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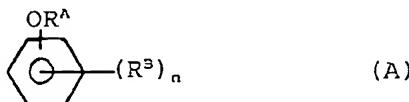
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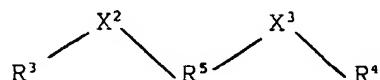
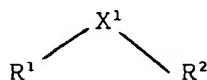
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(54) Chlorination of aromatic compounds and catalysts therefor

(57) A process for the chlorination of an aromatic compound of the following formula (A):



wherein R^A is H or C₁ to C₁₂ alkyl, cycloalkyl, aryl, alkaryl, aralkyl or carboxyalkyl, the or each R^B independently is selected from H, C₁-C₄ alkyl (especially methyl), C₁-C₄ haloalkyl or polyhaloalkyl, e.g. C₁-C₄ perfluoroalkyl, C₁-C₄ alkoxy, C₅-C₁₂ aryl (e.g. phenyl), alkaryl or aralkyl, or halogen, n is an integer which is 0, 1 or 2, and the or each R^B, if present, may independently be attached at the ortho or the meta position (preferably at the meta-position), which process comprises reacting (preferably in homogeneous liquid phase below 35°C) the aromatic compound (which is preferably phenol) with a chlorinating agent (preferably sulphuryl chloride) in the presence of a sulphur-containing catalyst, optionally also in the presence of a Lewis acid co-catalyst, characterised in that the sulphur-containing catalyst is a compound according to the following formula (I) or formula (II):



in which:

each of X¹, X², and X³ is independently selected from the group consisting of: S, SO, SO₂;

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R¹ is selected from the group consisting of:

optionally substituted straight or branched chain alkyl or alkanediyl having from 2 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;

R² is an optionally substituted straight or branched chain alkyl or alkanediyl group having from 1 to 20 carbon atoms;

R³ and R⁴ are each independently selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;

R⁵ is an optionally substituted straight or branched chain alkylene, arylene, alkarylene or arylalkylene group having from 1 to 20 carbon atoms;

wherein in the above definitions of R¹, R², R³, R⁴ and R⁵ the optional substituents may be independently selected from the following: halogen (e.g. F, Cl), hydroxy, amino, cyano, nitro, C₁-C₄ alkyl, C₁-C₄ haloalkyl e.g. C₁-C₄ perfluoroalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy carbonyl.

Description

5 The present invention relates to the chlorination of aromatic compounds, particularly phenols, using certain sulphur-containing organic compounds as catalysts. The invention also relates to certain such sulphur-containing catalyst compounds per se and to processes for preparing them.

10 The regioselective mono-chlorination of phenols with sulphuryl chloride has been known since 1866, when DuBois demonstrated the treatment of molten phenol with an equimolar amount of sulphuryl chloride [Z.F.Chem. 705 (1866)]. Modern analytical techniques have shown that the reaction is not as selective as was thought by DuBois, with p-chlorophenol actually being the predominantly favoured product. More recently, the catalysis of this reaction by a combination of particular divalent sulphur compounds and metal halides has been disclosed in published US Patent No. 3920757 (Watson). One of the most preferred catalysts in this document is diphenyl sulphide, in combination with AlCl_3 , and this catalyst has been applied to a number of further chlorination reactions by sulphuryl chloride, giving a majority of para-mono-chlorinated product over the corresponding ortho-mono-chlorinated product.

15 This known catalyst system however has several disadvantages, particularly when intended for use on an industrial scale. For instance, product yields are not as great as may often be desired, coupled with the fact that only limited para:ortho chlorinated product ratios have hitherto been obtainable. (The para-mono-chlorinated products are generally the more useful industrially and are therefore preferred.) Also, the undesirable isomers and polychlorinated products hinder purification and can be costly to dispose of.

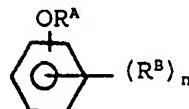
20 Another problem is that the known catalysts are difficult to separate from the reaction products mixture. Furthermore, the presence of AlCl_3 as a co-catalyst may be disadvantageous in that it hydrolyses on contact with water to produce acidic products which promote corrosion of metal reaction vessels and equipment. Many of these known sulphur-containing compounds also have a strong characteristic sulphurous odour, which necessitates more careful and expensive handling and equipment if health and safety hazards are to be avoided and worker-friendliness is to be optimised. Also, these known sulphur-containing catalysts are generally not re-usable, which may lead to problems of 25 safe and environmentally friendly disposal as well as of course being detrimental to the economics of the overall process.

25 The present invention aims to ameliorate at least some of the above disadvantages of the prior art by providing new sulphur-containing catalysts which are useful for catalysing the chlorination reaction of phenols using a chlorinating agent, which new catalysts not only give good product yields and high para-chlorinated product:orthochlorinated product (para:ortho) ratios, but may also be substantially odourless and may be easily recovered, hence leading to improved 30 economics of the process when applied industrially.

In a first aspect the present invention provides a process for the chlorination of an aromatic compound of the following formula (A):

35

(A)



40

45 wherein R^{A} is H or C_1 to C_{12} alkyl, cycloalkyl, aryl, alkaryl, aralkyl or carboxyalkyl, the or each R^{B} independently is selected from H, C_1 - C_4 alkyl (especially methyl), C_1 - C_4 haloalkyl or polyhaloalkyl, e.g. C_1 - C_4 perfluoroalkyl, C_1 - C_4 alkoxy, C_5 - C_{12} aryl (e.g. phenyl), alkaryl or aralkyl, or halogen, n is an integer which is 0, 1 or 2, and the or each R^{B} , if present, may independently be attached at the ortho or the meta position, preferably at the meta-position, the said process comprising reacting the aromatic compound with a chlorinating agent in the presence of a sulphur-containing catalyst, optionally also in the presence of a Lewis acid co-catalyst of the formula MX_m , where: M is a metal or metalloid such as B, Al, Ga, In, Ti, Ge, Sn, Cd, Ni, Fe, Zn, Ti, Hg, La; X is an electronegative group such as F, Cl, Br, I, C_1 - C_4 alkoxide, aryloxide e.g. phenoxide, carboxylate e.g. acetate, arencarboxylate e.g. benzoate, substituted carboxylate e.g. trifluoroacetate, C_1 - C_4 alkanesulphonate, arenesulphonate or substituted sulphonate e.g. trifluoromethanesulphonate; and m is an integer which is preferably 1, 2, 3 or 4; characterised in that the sulphur-containing catalyst is a compound according to the following formula (I) or formula (II):

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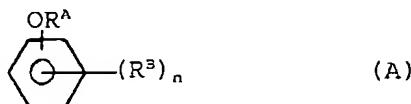
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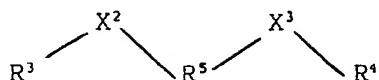
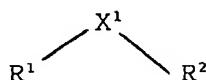
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R² is an optionally substituted straight or branched chain alkyl or alkanediyl group having from 1 to 20 carbon atoms;

R³ and R⁴ are each independently selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;

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The regioselective mono-chlorination of phenols with sulphuryl chloride has been known since 1866, when DuBois demonstrated the treatment of molten phenol with an equimolar amount of sulphuryl chloride [Z.F.Chem. 705 (1866)]. Modern analytical techniques have shown that the reaction is not as selective as was thought by DuBois, with *p*-chlorophenol actually being the predominantly favoured product. More recently, the catalysis of this reaction by a combination of particular divalent sulphur compounds and metal halides has been disclosed in published US Patent No. 3920757 (Watson). One of the most preferred catalysts in this document is diphenyl sulphide, in combination with AlCl_3 , and this catalyst has been applied to a number of further chlorination reactions by sulphuryl chloride, giving a majority of *para*-mono-chlorinated product over the corresponding *ortho*-mono-chlorinated product.

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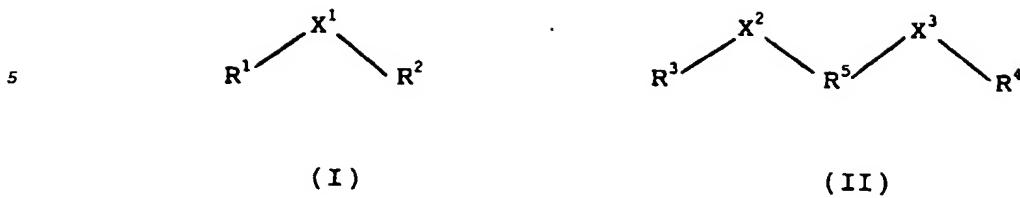
Another problem is that the known catalysts are difficult to separate from the reaction products mixture. Furthermore, the presence of AlCl_3 as a co-catalyst may be disadvantageous in that it hydrolyses on contact with water to produce acidic products which promote corrosion of metal reaction vessels and equipment. Many of these known sulphur-containing compounds also have a strong characteristic sulphurous odour, which necessitates more careful and expensive handling and equipment if health and safety hazards are to be avoided and worker-friendliness is to be optimised. Also, these known sulphur-containing catalysts are generally not re-usable, which may lead to problems of safe and environmentally friendly disposal as well as of course being detrimental to the economics of the overall process.

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In a first aspect the present invention provides a process for the chlorination of an aromatic compound of the following formula (A):



wherein R^A is H or C_1 to C_{12} alkyl, cycloalkyl, aryl, alkaryl, aralkyl or carboxyalkyl, the or each R^B independently is selected from H , C_1 - C_4 alkyl (especially methyl), C_1 - C_4 haloalkyl or polyhaloalkyl, e.g. C_1 - C_4 perfluoroalkyl, C_1 - C_4 alkoxy, C_5 - C_{12} aryl (e.g. phenyl), alkaryl or aralkyl, or halogen, n is an integer which is 0, 1 or 2, and the or each R^B , if present, may independently be attached at the *ortho* or the *meta* position, preferably at the *meta*-position, the said process comprising reacting the aromatic compound with a chlorinating agent in the presence of a sulphur-containing catalyst, optionally also in the presence of a Lewis acid co-catalyst of the formula MX_m , where: M is a metal or metalloid such as B , Al , Ga , In , Ti , Ge , Sn , Cd , Ni , Fe , Zn , Ti , Hg , La ; X is an electronegative group such as F , Cl , Br , I , C_1 - C_4 alkoxide, aryloxide e.g. phenoxide, carboxylate e.g. acetate, arencarboxylate e.g. benzoate, substituted carboxylate e.g. trifluoroacetate, C_1 - C_4 alkanesulphonate, arenesulphonate or substituted sulphonate e.g. trifluoromethanesulphonate; and m is an integer which is preferably 1, 2, 3 or 4; characterised in that the sulphur-containing catalyst is a compound according to the following formula (I) or formula (II):



in which:

15 each of X¹, X², and X³ is independently selected from the group consisting of: S, SO, SO₂;
 R¹ is selected from the group consisting of: optionally substituted straight or branched chain alkyl or alkanediyl having from 2 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;
 20 R² is an optionally substituted straight or branched chain alkyl or alkanediyl group having from 1 to 20 carbon atoms;
 R³ and R⁴ are each independently selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;
 25 R⁵ is an optionally substituted straight or branched chain alkylene, arylene, alkarylene or arylalkylene group having from 1 to 20 carbon atoms;

25 wherein in the above definitions of R¹, R², R³, R⁴ and R⁵ the optional substituents may be independently selected from the following: halogen (e.g. F, Cl), hydroxy, amino, cyano, nitro, C₁-C₄ alkyl, C₁-C₄ haloalkyl e.g. C₁-C₄ perfluoroalkyl, C₁-C₄ alkoxy, C₁-C₄ alkoxy carbonyl.

In a second aspect the present invention provides a sulphur-containing compound according to the above formula (I) or formula (II) (wherein X¹, X², X³, R¹, R², R³, R⁴ and R⁵ have the same meanings as above) especially for use as a catalyst in the chlorination of an aromatic compound of formula (A) above (wherein R^A, R^B and n have the same meanings as above) by a chlorinating agent, e.g. sulphuryl chloride.

In a third aspect the present invention provides the use of a sulphur-containing compound of the second aspect of the invention as a catalyst in the chlorination of an aromatic compound of formula (A) above by a chlorinating agent, e.g. sulphuryl chloride.

The above primary aspects of the invention, and preferred features and embodiments thereof, will now be described in further detail.

The chlorinating agent and the reaction conditions of the chlorination process

40 In the process according to the first aspect of the invention, the chlorinating agent is suitably sulphuryl chloride SO₂Cl₂. Other known chlorinating agents however may be suitable, e.g. chlorine gas. The process using sulphuryl chloride with the sulphur-containing catalyst, and with the optional presence of the Lewis acid co-catalyst, is preferably carried out in homogeneous liquid phase, without the presence of a solvent. However, a solvent may be used, if desired or necessary. Suitable solvents include alkanes such as n-hexane, THF, diethyl ether, halogenated hydrocarbons such as perchloroethylene or carbon tetrachloride, chloroform or dichloromethane, petrol ether, alcohols such as ethanol or methanol, water, pyridine, dimethylformamide, dimethylsulphoxide or the catalysts themselves, or mixtures of any of the aforesaid solvents. If a solvent is used, the temperature at which the reaction is carried out is generally lower than when there is no solvent present, e.g. if phenol is the aromatic compound to be chlorinated, then in the absence of solvent the reaction mixture may solidify at a temperature less than 35°C, which sets a practical lower limit on the possible temperature for the reaction.

50 For maximum selectivity it is preferable that the temperature used is as low as possible, e.g. even below 35°C, more preferably below about 20 or 25°C, even possibly down to about 0°C, but the reaction may however still work, in certain embodiments, at temperatures of as high as 85°C or more. Often the reaction will be carried out approximately at or near room temperature, e.g. in the region of about 15 to about 30°C, in order to minimise the external heating or cooling that is required.

55 The amount of sulphur-containing catalyst present in the reaction mixture is preferably between about 0.2 and about 10 mol%, with respect to the amount of the aromatic compound, but in the case where the catalyst acts as the

solvent, it is preferably present in large molar excess (e.g. at least 500 mol% excess, preferably at least 1000 mol% excess).

The amount of sulphuryl chloride (SO_2Cl_2) (or other chlorinating agent) present in the reaction mixture may also vary, e.g. depending on the amount of aromatic compound to be reacted and whether a solvent is used. Preferably the SO_2Cl_2 is present in small excess with respect to the amount of the aromatic compound, e.g. up to about 100 mol% excess. If desired or necessary, it may be possible for the SO_2Cl_2 to be present in molar deficit, e.g. up to about 20 mol% deficit. The most preferred amount of SO_2Cl_2 present in the reaction mixture is approximately at a 2 to 20 mol% excess over the amount of aromatic compound.

The chlorination reaction may be carried out by the slow addition of the SO_2Cl_2 to a reaction mixture consisting of or containing the aromatic compound, the sulphur-containing catalyst, the Lewis acid co-catalyst (if present) and the solvent (if present). Following the addition a period of stirring is generally used to ensure that the reaction is substantially complete, whilst minimising cost.

The optional presence of the above defined Lewis acid co-catalyst in the reaction mixture may further increase the para:ortho product ratio and also the yield of the mono-chlorinated product. However, in certain industrial processes the presence of such a Lewis acid may cause a problem as regards corrosion of equipment hardware and in its separation from effluent streams, so in certain practical embodiments of the process of the invention the use of a Lewis acid co-catalyst may be less desirable. A metal halide such as AlCl_3 is often the most selective and thus preferable Lewis acid, although others may perform reasonably well. Both FeCl_3 and ZnCl_2 for instance have fewer practical and environmental disadvantages than AlCl_3 for large scale use. When used, the amount of Lewis acid in the reaction mixture (in relation to the amount of the aromatic compound) may vary between approximately 0.1 and 15 mol%, with the preferred amount being about at a 1 to 40 mol% excess over the amount of sulphur-containing catalyst used.

The scale of the chlorination process may vary, one advantage of the invention being that having a larger scale process may not deleteriously affect the para:ortho product ratio or the overall yield of the desired -product from the reaction.

The sulphur-containing catalyst compounds

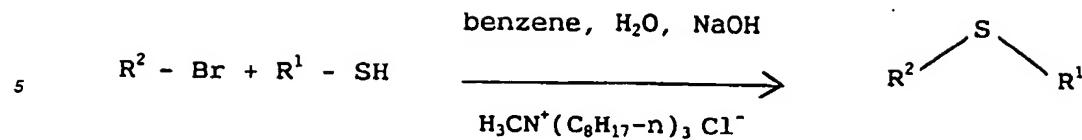
In embodiments of the invention where the sulphur-containing catalyst used is one according to general formula (I), X^1 in the formula is preferably either S or SO, and is most preferably S. Without being bound by any particular theory, it is believed that when the S atom is in a higher oxidation state, it is initially chlorinated by sulphuryl chloride less well and thus is less able to promote chlorination of the aromatic compound, resulting in less efficient functioning as a catalyst.

In embodiments where the sulphur-containing catalyst is a compound of formula (I), the catalyst compound may be symmetrical or unsymmetrical. It is preferred in symmetrical, unbranched dialkyl sulphides that the alkyl groups R^1 and R^2 each independently contain from 2 to 16 carbon atoms, more preferably 4 or 5 carbon atoms each. In symmetrical, branched dialkyl sulphides it is also preferred that the alkyl groups R^1 and R^2 each independently contain from 2 to 16 carbon atoms, but more preferably 3 or 4 carbon atoms each, with iso-propyl or sec-butyl being most preferred. Without being bound by any particular theory, it is believed that it is the steric bulk of the groups attached to the central sulphur atom of the catalyst compound that primarily controls the catalyst's activity.

Less preferred, but still useful, examples of catalyst compounds of formula (I) are those which are unsymmetrical, i.e. in which R^1 and R^2 are different. One group of preferred catalysts in this class is those with one of R^1 and R^2 being n-butyl and the other of R^1 and R^2 containing 2 to 4 carbon atoms, more particularly being selected from iso-propyl, sec-butyl, and iso-butyl. Another group of preferred catalysts in this class are those with one of R^1 and R^2 being phenyl, and the other of R^1 and R^2 being an unbranched alkyl group having 1 to 3 carbon atoms. Again, without being bound by any particular theory, it is thought that the steric bulk of the groups R^1 and R^2 is what primarily controls these catalysts' activities.

The above symmetrical and unsymmetrical sulphide compounds of formula (I) may be synthesised in a known manner by the use of a phase transfer catalyst. For example, a haloalkane is reacted with a thiol in the presence of methyltriocetyl ammonium chloride in a benzene, water and sodium hydroxide mixture to yield the desired compound.

This synthesis can be represented by the equation:



10 Turning to sulphur-containing catalysts with the above general formula (II), in embodiments of the invention where the catalyst is a compound according to formula (II), preferably both of the groups X^2 and X^3 are S. Compounds of general formula (II) generally will have a higher molecular weight than compounds of general formula (I), and hence will generally produce catalysts having less sulphurous odour and which are easier to separate from the reaction products mixture by virtue of their generally higher boiling points, as compared with many of the compounds of general formula (I).

In the above formula (II), preferably R^5 is an unsubstituted alkanediyl group, and more preferably it is straight chained. In compounds of formula (II) in which R^5 is an unbranched, unsubstituted alkanediyl group, it is preferred that it contains from 4 to 12 carbon atoms, most preferably from 7 to 12 carbon atoms.

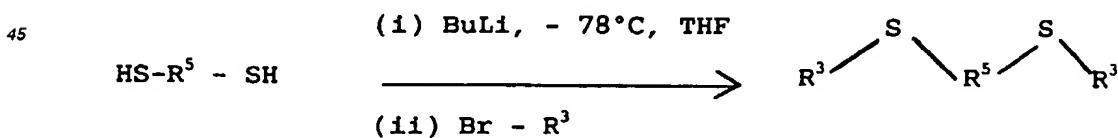
The groups R^3 and R^4 may have either the same or different carbon atom frameworks. In compounds of formula (II) in which R^3 and R^4 have the same carbon atom framework, both groups may be unbranched and/or unsubstituted. Preferably, both groups are unbranched and unsubstituted and independently contain from 1 to 7 carbon atoms.

25 In compounds of formula (II) in which R³ and R⁴ have different carbon atom frameworks, R³ is preferably selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms and optionally substituted aryl having from 5 to 20 carbon atoms, and R⁴ is different from R³ and is preferably selected from the group consisting of: optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms. Both R³ and R⁴ may be unsubstituted, and preferably R³ is selected from H, unbranched C₁ - C₄ alkyl, or phenyl, and R⁴ is selected from C₄ to C₇ alkyl, phenyl or benzyl.

30 Symmetrical dithia- compounds of formula (II) may be synthesised by any one of the following three exemplary methods (Methods A, B and C), of which Method C can also be used to synthesise the unsymmetrical dithia- compounds of formula (II). For the sake of simplicity, the three methods are exemplified below with reference to simple dithia-alkanes only, but analogous methods can be readily applied to more complicated analogous compounds also of formula (II), as the person skilled in the art will readily appreciate.

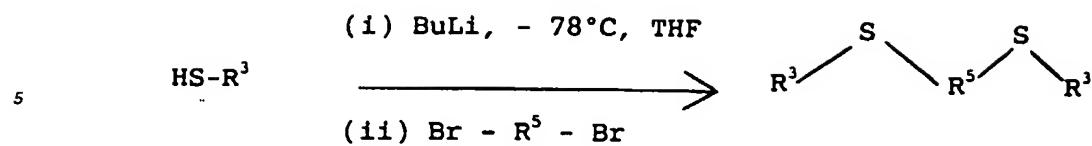
35 Method A

40 In this method one mole equivalent of dithiol of the formula $\text{HS-R}^5\text{-SH}$ is lithiated, e.g. with BuLi at -78°C in THF , and is then reacted with two mole equivalents of bromoalkane of formula Br-R^3 to produce the required symmetrical dithia-alkane, $\text{R}^3\text{-S-R}^5\text{-S-R}^3$, wherein R^4 in the general formula (II) is the same as R^3 . This synthesis can be represented by the following equation:



Method B

55 In this method two mole equivalents of thiol of the formula HS-R^3 are lithiated, e.g. with BuLi at -78°C in THF, and are then reacted with dibromoalkane of the formula $\text{Br-R}^5\text{-Br}$ to produce the required symmetrical dithia-alkane, $\text{R}^3\text{-S-R}^5\text{-S-R}^3$, wherein R^4 in the general formula (II) is the same as R^3 . This synthesis can be represented by the following equation:

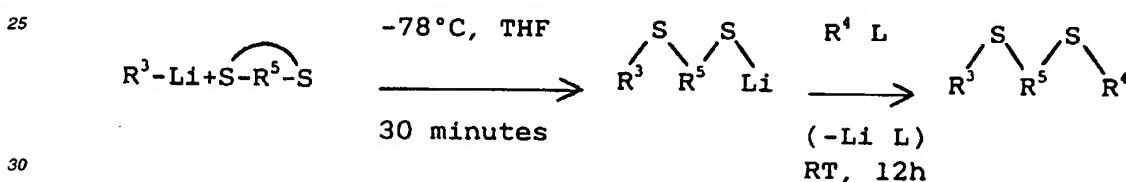


Method C

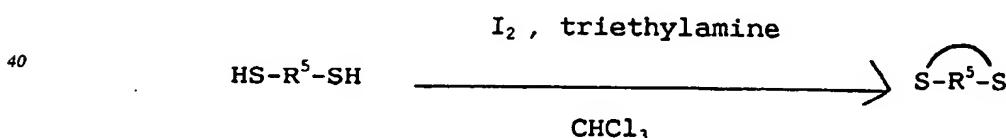
10 In this method a cyclic disulphide (see below) of the formula



is first reacted with one equivalent of an organolithium reagent of the formula $R^3\text{-Li}$, e.g. at -78°C in THF for 30 minutes, to produce an intermediate of the formula $R^3\text{-S-}R^5\text{-S-Li}$. This intermediate is then trapped with an electrophile of the formula $R^4\text{-L}$, wherein L is any suitable leaving group such as halide (e.g. Cl^- , Br^-) or carboxylate or sulphonate, under appropriate conditions e.g. at room temperature for 12 hours, to produce the required dithia-alkane of the formula $R^3\text{-S-}R^5\text{-S-}R^4$. This synthesis can be represented by the following equation:



35 Cyclic disulphides, and more particularly 1,2-dithiacycloalkanes of ring sizes from 5 to 12, for use in Method C above may be readily synthesised by oxidative cyclisation of the readily available dithiols according to well known literature procedures, e.g. using as reagents iodine and triethylamine in trichloromethane, which reaction can be represented by the following equation:

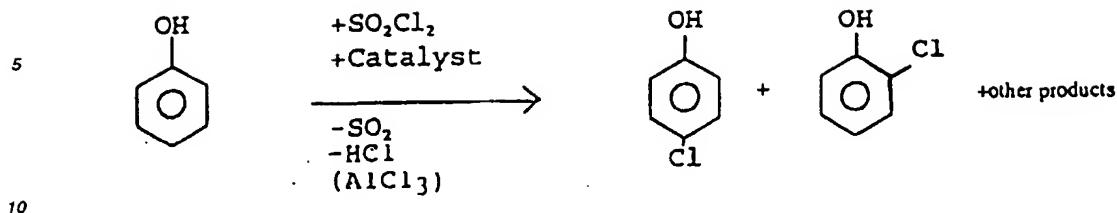


45 EXAMPLES

Preferred features and embodiments of the present invention in its various aspects will now be illustrated in detail by way of the following examples.

50 Comparative Example 1 and Examples 1 to 9

In the following Comparative Example 1 and Examples 1 to 9 the following reaction:



is carried out as follows:

A clean and dry 250ml two necked, round bottom flask is flushed with N₂ for a few seconds, to prevent oxidation of phenol and hydrolysis of AlCl₃, if present. 100mmol (9.41g) of phenol is then placed in the flask along with 2.69mmol of the catalyst used, 3.75mmol AlCl₃ if required and a magnetic follower. The flask is fitted with a stopper and a pressure equalising dropping funnel. The flask is placed in an oil-bath set at 60°C to melt the phenol. 110mmol (8.8ml) of freshly distilled sulphuryl chloride (see below) is placed in the dropping funnel and the funnel is fitted with a CaCl₂ drying tube. When the phenol is molten the flask is transferred to an oil-bath which is kept at 35°C on a hot plate magnetic stirrer equipped with a contact thermometer. The reaction mixture is stirred while the SO₂Cl₂ is added with a rate of approximately one drop every two seconds. The addition rate is checked from time to time and the addition is finished within two hours. Stirring is then maintained for another 2 hours.

The reaction is quenched with 30ml of distilled water and stirred for 30 minutes to hydrolyse residual SO₂Cl₂. The two phases are transferred into a separating funnel and the flask rinsed with distilled water and diethyl ether. The mixture is extracted twice with 30ml of diethyl ether and the combined ether layers are washed with 10ml of distilled water. The organic phase is then dried over MgSO₄ and filtered. The organic phase is evaporated under vacuum (18 mbar) at 50°C. The product is then subjected to elemental analysis and analysed by gas chromatography, as described further below.

The freshly distilled sulphuryl chloride mentioned above is prepared by placing sulphuryl chloride in a double-necked, round-bottom flask with a few anti-bumping granules. The flask is set up for distillation and fitted with a nitrogen inlet and a water-cooled condenser leading to a three way receiver and a nitrogen outlet. The gas flows out through a scrubber. The system is flushed with nitrogen and then the gas flow is halted. The flask is heated and the fraction boiling at 67-69°C is collected as sulphuryl chloride. This colourless liquid is stored under nitrogen.

In order to analyse the purified reaction products, a precisely known amount of the stored sample (approximately 500mg) and 100mg tetradecane as internal standard are weighed into a flask and diluted with 25ml dichloromethane. 1μl of the resulting solution is injected onto a gas chromatograph for analysis.

The gas chromatography system used involves a Philips PU 4400 instrument with a PU 4920 data station providing control, data storage and manipulation for the gas chromatograph. The conditions set for analysis are:

| | | |
|----|---------------------------|--|
| 40 | column: | 15m carbowax megabore, ID 0.54mm, 1.2μm film thickness |
| | carrier gas: | 5ml/min helium |
| | make up gas: | 25ml/min nitrogen |
| 45 | injector temperature: | 300°C |
| | detector temperature: | 300°C (F.I.D.) |
| | injection technique: | splitless |
| | initial time: | 2 minutes |
| 50 | column start temperature: | 35°C |
| | ramp rate: | 20°C/min |
| | upper temperature: | 240°C |

The trace produced by the gas chromatograph is converted into mol% of product present in the purified reaction products using standard calculations as are well known and commonly applied in the art.

55 Comparative Example 1

Tables A and B below illustrate the results of reactions of phenol with SO₂Cl₂ using a variety of sulphur containing

catalysts, some of which are known in the prior art and some of which are in accordance with the invention, respectively without (Table A) and with (Table B) the presence of AlCl_3 . The catalysts marked with an asterisk are known from the prior art.

5 In Tables A and B below, as in other results Tables presented from here onwards in this specification, all percentage yields of products have been normalised to 100% total mass balance. Actual mass balances calculated are given in a separate column. In certain other results Tables the actual calculated yields are given for all components. In these cases, footnotes are used to indicate the different method of presentation.

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Table A

| catalyst | mol % phenol | mol % ortho-chlorophenol | mol % para-chlorophenol | mol % dl-chlorophenol | p / o-ratio | mass balance % |
|---------------------------|--------------|--------------------------|-------------------------|-----------------------|-------------|----------------|
| no catalyst | * | 29.2 | 12.2 | 58.2 | 0.4 | 4.8 |
| diphenyl sulfide | * | 8.7 | 13.0 | 74.0 | 4.4 | 5.7 |
| cyclohexyl methyl sulfide | 7.3 | 9.2 | 82.0 | 1.4 | 8.9 | 94.4 |
| benzyl phenyl sulfide | 3.0 | 8.9 | 85.7 | 2.4 | 9.7 | 100.0 |
| dibenzyl sulfide | * | 4.4 | 11.9 | 86.8 | 2.5 | 6.8 |
| 2-(phenylthio)-ethanol | 15.7 | 16.5 | 64.3 | 3.5 | 3.9 | 100.0 |
| thiophenoxyacetic acid | 1.5 | 13.1 | 82.7 | 2.7 | 6.3 | 89.0 |
| thiophenol | * | 6.5 | 12.0 | 78.9 | 2.5 | 6.6 |
| diphenyl disulfide | * | 4.6 | 9.4 | 82.5 | 3.6 | 8.8 |
| thiophene | * | 14.9 | 13.1 | 71.6 | 0.5 | 5.5 |
| | | | | | | 100.0 |

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table B

| catalyst | mol % phenol | mol % ortho-chlorophenol | mol % para-chlorophenol | mol % di-chlorophenol | p/o-ratio | mass balance % |
|---------------------------|--------------|--------------------------|-------------------------|-----------------------|-----------|----------------|
| no catalyst | 4 | 2.8 | 15.3 | 81.2 | 0.7 | 5.3 |
| diphenyl sulfide | 4 | 8.0 | 12.2 | 77.4 | 2.3 | 6.3 |
| cyclohexyl methyl sulfide | 8.9 | 7.5 | 81.9 | 1.6 | 10.9 | 100.0 |
| benzyl phenyl sulfide | 0.1 | 9.7 | 84.5 | 5.6 | 8.7 | 100.0 |
| dibenzyl sulfide | 4 | 0.4 | 9.0 | 88.1 | 2.3 | 9.7 |
| 2-(phenyllthio)-ethanol | 12.4 | 10.1 | 75.6 | 1.9 | 7.5 | 94.8 |
| thiophenoxyacetic acid | 2.2 | 9.8 | 86.1 | 2.0 | 8.8 | 92.5 |
| thiophenol | 4 | 0.6 | 11.3 | 85.1 | 2.6 | 7.5 |
| diphenyl sulfide | 4 | 12.1 | 11.4 | 74.3 | 2.2 | 6.5 |
| thiophene | 4 | 3.6 | 9.5 | 84.5 | 2.4 | 8.9 |
| | | | | | 99.4 | |

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Example 1

5 Table 1 below illustrates the results of reactions of phenol with SO_2Cl_2 with various straight chain symmetrical dialkyl sulphides, with and without the presence of AlCl_3 . Except for dimethyl sulphide, all of the exemplified dialkyl sulphides catalyse the chlorination of phenol by SO_2Cl_2 better than diphenyl sulphide (see Comparative Example 1). The para:ortho ratio of monochlorophenols peaks with straight chain dialkyl sulphides at an overall chain length of C_8 to C_{10} . The amount of phenol remaining after the reaction also shows a similar trend.

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Table 1: Chlorination of phenol in the presence of dialkyl sulfides^a

| catalyst | presence of AlCl_3 | phenol (P) mol% | <i>ortho</i> -chlorophenol (OCP) mol% ^b | <i>para</i> -chlorophenol (PCP) mol% ^b | dichlorophenol (DCP) mol% ^b | p/o ratio | mass balance % |
|------------------------|-----------------------------|--------------------|--|---|--|-----------|-------------------|
| dimethyl sulfide | - | 12.0 | 24.9 | 61.0 | 2.1 | 2.4 | 100.0 |
| di-ethyl sulfide | - | 1.2 | 13.0 | 84.2 | 1.6 | 6.5 | 100.0 |
| di-ethyl sulfide | ✓ | 0.9 | 8.6 | 84.0 | 0.9 | 9.8 | 94.4 |
| di-n-propyl sulfide | - | 7.1 | 9.7 | 81.6 | 1.5 | 8.4 | 99.9 |
| di-n-propyl sulfide | ✓ | 8.7 | 6.0 | 83.2 | 0.4 | 13.9 | 98.3 |
| di-n-butyl sulfide | - | 5.3 | 8.5 | 82.9 | 1.0 | 9.8 | 97.7 |
| di-n-butyl sulfide | ✓ | 0.0 | 5.4 | 86.6 | 3.2 | 16.0 | 95.2 |
| di-n-pentyl sulfide | - | 12.2 | 8.4 | 76.6 | 0.9 | 9.1 | 98.1 |
| di-n-pentyl sulfide | ✓ | 10.8 | 5.8 | 77.7 | 0.6 | 13.6 | 94.9 |
| di-n-hexyl sulfide | - | 8.9 | 9.4 | 72.3 | 1.0 | 7.7 | 91.6 |
| di-n-hexadecyl sulfide | - | 14.1 | 8.9 | 62.7 | 0.9 | 7.0 | 86.6 |

a) 100 mmol of phenol, 110 mmol SO_3Cl_2 , 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of P+OCP+PCP + DCP; low mass balance indicates either physical loss of material or the production of other materials

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Example 2

Table 2 below illustrates the results of reactions of phenol with SO_2Cl_2 with various symmetrical or unsymmetrical, linear or branched chain dialkyl sulphides, with and without the presence of AlCl_3 , in accordance with the invention.

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Table 2: Chlorination of phenol in the presence of dialkyl sulfides^a

| catalyst | presence of AlCl ₃ | phenol (P) mol % | o/t/o-chlorophenol (OCP) mol % ^b | p-chorophenol (FCP) mol % ^b | dichlorophenol (DCP) mol % ^b | p/o ratio | mass balance % |
|----------------------------|----------------------------------|------------------------|---|--|---|-----------|----------------------|
| di-isoo-propyl sulfide | - | 7.1 | 9.7 | 81.6 | 1.5 | 8.4 | 99.9 |
| di-iso-propyl sulfide | ✓ | 8.7 | 6.0 | 83.2 | 0.4 | 13.9 | 98.3 |
| di-sec-butyl sulfide | - | 11.1 | 9.0 | 76.8 | 1.4 | 8.5 | 98.3 |
| di-sec-butyl sulfide | ✓ | 9.4 | 5.7 | 82.4 | 0.4 | 14.4 | 97.9 |
| di-tert-butyl sulfide | - | 8.6 | 10.6 | 68.2 | 3.5 | 6.4 | 90.9 |
| di-tert-butyl sulfide | ✓ | 12.6 | 9.4 | 65.5 | 6.4 | 7.0 | 93.9 |
| n-butyl methyl sulfide | - | 14.9 | 16.2 | 67.5 | 1.4 | 4.2 | 100.0 |
| n-butyl methyl sulfide | ✓ | 13.5 | 13.6 | 71.9 | 1.0 | 5.3 | 100.0 |
| n-butyl-iso-propyl sulfide | - | 17.4 | 7.3 | 72.0 | 0.6 | 9.9 | 97.3 |
| n-butyl-iso-propyl sulfide | ✓ | 11.0 | 4.8 | 80.6 | 0.7 | 16.8 | 97.1 |
| n-butyl-sec-butyl sulfide | - | 17.2 | 8.3 | 70.4 | 0.6 | 8.5 | 96.5 |
| n-butyl-sec-butyl sulfide | ✓ | 12.6 | 5.1 | 78.9 | 0.1 | 15.7 | 96.7 |
| n-butyl-iso-butyl sulfide | - | 15.4 | 7.8 | 73.0 | 0.7 | 9.3 | 96.9 |
| n-butyl-iso-butyl sulfide | ✓ | 12.5 | 5.1 | 76.1 | 0.3 | 15.1 | 94.0 |
| n-butyl-tert-butyl sulfide | - | 7.1 | 13.3 | 74.0 | 0.8 | 5.5 | 95.2 |
| n-butyl-tert-butyl sulfide | ✓ | 10.8 | 8.0 | 73.8 | 3.0 | 9.2 | 95.6 |

a) 100 mmol phenol, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of P+OCP+PCP + DCP; low mass balance indicates either physical loss of material or the production of other materials

Example 3

Table 3 below illustrates the results of reactions of meta-cresol with SO_2Cl_2 with various symmetrical linear or branched chain dialkyl sulphides, with and without the presence of AlCl_3 , in accordance with the invention.

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Table 3: Chlorination of *meta*-cresol in the presence of various sulfur compounds^a

| catalyst | presence of AlCl ₃ | MC mol% | OCMC mol% ^b | PCMC mol% ^b | p/o ratio | mass balance % |
|-----------------------|----------------------------------|------------|---------------------------|---------------------------|-----------|-------------------|
| di-n-propyl sulfide | - | 5.6 | 8.0 | 84.2 | 10.5 | 97.8 |
| di-n-propyl sulfide | ✓ | 5.6 | 6.0 | 83.6 | 14.0 | 95.2 |
| di-iso-propyl sulfide | - | 13.1 | 7.3 | 71.3 | 9.7 | 91.7 |
| di-iso-propyl sulfide | ✓ | 5.0 | 5.1 | 83.0 | 16.1 | 93.1 |
| di-n-butyl sulfide | - | 5.2 | 5.8 | 79.0 | 13.6 | 90.0 |
| di-n-butyl sulfide | ✓ | 1.1 | 5.4 | 93.2 | 17.3 | 99.7 |
| di-n-pentyl sulfide | - | 3.4 | 6.7 | 85.1 | 12.8 | 95.2 |
| di-n-pentyl sulfide | ✓ | 3.9 | 5.5 | 85.3 | 15.5 | 94.7 |
| di-n-hexyl sulfide | - | 5.2 | 7.6 | 83.1 | 11.0 | 95.9 |
| di-n-hexyl sulfide | ✓ | 4.2 | 5.2 | 83.6 | 16.1 | 93.0 |

a) 100 mmol MC, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

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Example 4

5 Table 4 below illustrates the results of reactions of meta-cresol with SO_2Cl_2 with various symmetrical or unsymmetrical linear or branched chain dialkyl sulphides, with and without the presence of AlCl_3 , in accordance with the invention.

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Table 4: Chlorination of *meta*-cresol in the presence of various sulfur compounds^a

| catalyst | presence of AlCl_3 | MC mol % | OCMC mol % ^b | PCMC mol % ^b | p/o ratio | mass balance % |
|----------------------------|--------------------------------|-------------|----------------------------|----------------------------|-----------|-------------------|
| methyl n-nonyl sulfide | - | 14.5 | 7.6 | 77.9 | 10.3 | 100.0 |
| ethyl n-octyl sulfide | - | 8.0 | 7.0 | 85.0 | 11.4 | 100.0 |
| n-propyl n-heptyl sulfide | - | 7.7 | 6.0 | 73.1 | 12.2 | 86.8 |
| n-butyl n-hexyl sulfide | - | 8.6 | 7.3 | 69.8 | 9.6 | 85.7 |
| n-butyl iso-butyl sulfide | - | 6.0 | 8.0 | 82.1 | 10.3 | 96.1 |
| n-butyl iso-butyl sulfide | ✓ | 3.6 | 5.1 | 87.3 | 17.1 | 96.0 |
| n-butyl sec-butyl sulfide | - | 7.9 | 7.3 | 80.4 | 11.0 | 95.6 |
| n-butyl sec-butyl sulfide | ✓ | 7.5 | 4.9 | 84.0 | 17.1 | 96.4 |
| n-butyl tert-butyl sulfide | - | 8.3 | 12.0 | 68.4 | 5.7 | 88.7 |
| n-butyl tert-butyl sulfide | ✓ | 5.7 | 8.8 | 76.1 | 8.6 | 90.6 |
| di-n-butyl sulfoxide | - | 4.0 | 7.4 | 68.0 | 9.2 | 79.4 |
| di-n-butyl sulfide | ✓ | 10.8 | 6.2 | 69.4 | 11.2 | 86.4 |
| di-n-butyl sulfone | - | 5.8 | 9.8 | 81.8 | 8.3 | 97.4 |
| di-n-butyl sulfone | ✓ | 2.4 | 9.6 | 83.6 | 8.7 | 95.6 |

a) 100 mmol MC, 110 mmol SO_2Cl_2 , 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

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The next set of examples (Examples 5 to 9) illustrate the effect of changing various reaction parameters on the effectiveness of the catalysed reaction. The reactions were carried out under the same conditions as detailed above except for the parameter in question being varied, with di-iso-propyl sulphide as the catalyst, and without the presence of AlCl_3 .

5 Example 5

In this example the reaction temperature is varied between 35°C and 85°C (see Table 5 below). As the temperature increases both the para:ortho ratio and the mol% of parachlorophenol drops, illustrating that the lower the temperature, the more selective is the reaction.

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Table 5

| temperature | mol % mono- chlorophenol | p/o-ratio | mol % phenol | mol % di- chlorophenol | mol % ortho- chlorophenol | mol % para- chlorophenol | mass balance % |
|-------------|-----------------------------|-----------|-----------------|---------------------------|------------------------------|-----------------------------|----------------|
| 35 | 86.0 | 9.8 | 12.8 | 1.1 | 8.0 | 78.1 | 96.2 |
| 45 | 80.0 | 7.7 | 18.2 | 1.8 | 9.1 | 70.9 | 97.8 |
| 55 | 78.9 | 5.5 | 18.7 | 2.4 | 12.1 | 66.8 | 86.1 |
| 65 | 79.2 | 4.0 | 18.9 | 1.9 | 16.0 | 63.2 | 100.0 |
| 75 | 71.9 | 3.6 | 25.2 | 3.0 | 15.6 | 56.2 | 100.0 |
| 85 | 68.4 | 3.5 | 28.0 | 3.7 | 15.1 | 53.2 | 95.3 |

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Example 6

In this example the amount of sulphuryl chloride added to the reaction mixture is varied between 80mmol and 200mmol (see Table 6 below). The most preferable amount is a 20 mol% excess with respect to the amount of phenol.

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Table 5

| mmol sulfonyl chloride | mol % mono- chlorophenol | p/o-ratio | mol % phenol | mol % di- chlorophenol | mol% ortho- chlorophenol | mol % para- chlorophenol | mass balance % |
|---------------------------|-----------------------------|-----------|-----------------|---------------------------|-----------------------------|-----------------------------|----------------|
| 80 | 58.7 | 8.8 | 40.4 | 0.9 | 5.9 | 52.8 | 94.3 |
| 90 | 67.3 | 8.5 | 31.9 | 0.8 | 7.1 | 60.2 | 96.6 |
| 100 | 78.5 | 10.5 | 20.7 | 0.7 | 6.8 | 71.8 | 95.8 |
| 110 | 86.0 | 9.8 | 12.8 | 1.1 | 8.0 | 78.1 | 96.2 |
| 120 | 93.1 | 9.7 | 5.3 | 1.6 | 8.7 | 84.4 | 96.9 |
| 150 | 70.3 | 8.1 | 0.1 | 29.6 | 7.8 | 62.5 | 95.3 |
| 200 | 35.0 | 5.7 | 0.4 | 64.6 | 5.2 | 29.8 | 70.0 |

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Example 7

5 In this example the amount of catalyst in the reaction mixture is varied between 0.5 mmol and 5.0 mmol (see Table 7 below). There are only small changes in the effectiveness of the catalyst dependent on the amount present, so the exact amount of catalyst in any reaction mixture is not crucial.

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Table 7

| mmol catalyst | mol % mono- chlorophenol | p/o-ratio | mol % phenol | mol % di- chlorophenol | mol% ortho- chlorophenol | mol % para- chlorophenol | mass balance % |
|------------------|-----------------------------|-----------|-----------------|---------------------------|-----------------------------|-----------------------------|----------------|
| 0.5 | 85.3 | 6.8 | 13.1 | 1.5 | 11.0 | 74.4 | 97.9 |
| 1.0 | 87.5 | 8.0 | 11.0 | 1.5 | 9.8 | 77.7 | 92.0 |
| 1.5 | 89.8 | 8.6 | 9.2 | 1.0 | 9.3 | 80.5 | 95.4 |
| 2.0 | 87.7 | 8.5 | 11.3 | 1.1 | 9.2 | 78.4 | 94.0 |
| 2.7 | 86.0 | 9.8 | 12.8 | 1.1 | 8.0 | 78.1 | 96.2 |
| 3.0 | 85.1 | 8.1 | 14.8 | 0.1 | 9.3 | 75.8 | 100.0 |
| 5.0 | 81.8 | 8.6 | 17.6 | 0.5 | 8.6 | 73.3 | 90.3 |

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Example 8

5 In this example the addition time of the sulphuryl chloride to the reaction mixture is altered between 0.5 hours and 4.5 hours (see Table 8 below). As with the amount of catalyst, the addition speed is not crucial to the effectiveness of the reaction.

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Table 8

| addition time in hours | mol % mono- chlorophenol | p/o-ratio | mol % phenol | mol % di- chlorophenol | mol% ortho- chlorophenol | mol % para- chlorophenol | mass balance % |
|---------------------------|-----------------------------|-----------|-----------------|---------------------------|-----------------------------|-----------------------------|----------------|
| 0.5 | 91.0 | 8.4 | 9.1 | 0.5 | 10.1 | 80.3 | 88.0 |
| 1.0 | 89.4 | 9.3 | 10.0 | 0.6 | 8.6 | 80.8 | 96.8 |
| 2.0 | 86.0 | 9.8 | 12.8 | 1.1 | 8.0 | 78.1 | 96.2 |
| 4.5 | 89.2 | 9.0 | 14.8 | 1.1 | 8.4 | 75.7 | 93.6 |

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Example 9

In this example the reaction is carried out in various solvents (see Tables 9a and 9b below), most of the reactions being carried out at two different temperatures, i.e. 0°C and 35°C. The reactions are carried out using a minimum amount of solvent, as solvent would be a disadvantage for industrial purposes. If precipitation occurs during the addition of the sulphuryl chloride when the reaction is being carried out at 0°C, the addition is stopped, the reaction mixture warmed up to room temperature where a liquid phase is obtained again, then the reaction vessel is replaced in the ice bath and the addition continued.

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Table 2a

| solvent | dielectric constant | temp. in °C | mol % phenol | mol % ortho-chlorophenol | mol % para-chlorophenol | mol % di-chlorophenol | p/o ratio | mass balance % |
|----------------------|---------------------|-------------|--------------|--------------------------|-------------------------|-----------------------|-----------|----------------|
| n-hexane | 1.89 / 20°C | 0 | 2.6 | 15.9 | 80.7 | 0.8 | 5.1 | 96.2 |
| n-hexane | 1.89 / 20°C | 35 | 5.3 | 10.7 | 83.2 | 0.8 | 7.8 | 90.8 |
| carbon tetrachloride | 2.24 / 20°C | 0 | 22.6 | 13.1 | 63.9 | 0.4 | 4.9 | 94.1 |
| carbon tetrachloride | 2.24 / 20°C | 35 | 8.2 | 9.0 | 82.3 | 0.5 | 9.1 | 91.4 |
| diethyl ether | 4.33 / 25°C | 0 | 1.6 | 17.0 | 80.5 | 0.9 | 5.4 | 83.0 |
| diethyl ether | 4.33 / 25°C | 35 | 7.1 | 15.2 | 77.1 | 0.6 | 5.1 | 90.2 |
| chloroform | 4.81 / 20°C | 0 | 2.4 | 12.9 | 84.0 | 0.7 | 6.5 | 94.0 |
| chloroform | 4.81 / 20°C | 35 | 5.5 | 8.5 | 85.6 | 0.4 | 10.1 | 89.0 |
| dichloromethane | 9.08 / 20°C | 0 | 1.9 | 17.2 | 80.2 | 0.7 | 4.6 | 92.2 |
| dichloromethane | 9.08 / 20°C | 35 | 9.4 | 11.3 | 78.3 | 1.0 | 7.0 | 87.8 |
| petrol ether 30-40°C | - | 0 | 4.9 | 13.6 | 81.1 | 0.4 | 6.0 | 95.1 |
| petrol ether 30-40°C | - | 35 | 13.0 | 7.9 | 78.5 | 0.6 | 9.7 | 92.3 |

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Table 2b

| solvent | dielectric constant | temp. in °C | amount in g | mol % phenol | mol % ortho-chlorophenol | mol % para-chlorophenol | mol % di-chlorophenol | p/o ratio | mass balance % |
|-----------------------|---------------------|-------------|-------------|--------------|--------------------------|-------------------------|-----------------------|-----------|----------------|
| water | 75.5 / 25 °C | 0 | 1.00 | 11.1 | 24.8 | 56.9 | 1.0 | 2.3 | 93.7 |
| di-iso-propyl sulfide | - | 0 | 2.03 | 5.7 | 5.3 | 74.9 | 0.3 | 14.1 | 87.0 |
| di-n-butyl sulfide | - | 0 | 1.94 | 5.8 | 7.2 | 70.8 | 0.1 | 9.8 | 84.0 |

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Although water hydrolyses sulphuryl chloride, it can act as a solvent, as the hydrolysis reaction is much slower than the chlorination reaction. The use of the catalysts as solvents is not preferred due to the relative expensiveness of these compounds.

5 Comparative Examples 2 and 3

The two following Comparative Examples 2 and 3 illustrate the use of sulphur-containing catalysts with general formula (I) for the chlorination of two alkyl-phenols, meta-cresol and meta-xyleneol. The reaction conditions are the same as for Comparative Example 1 above, except that 100mmol of the relevant alkyl-phenol is used.

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Comparative Example 2

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Tables C and D below illustrate the use of four sulphur-containing catalysts with the general formula (I), respectively with (Table C) and without (Table D) the presence of AlCl_3 , in comparison with no catalyst and diphenyl sulphide which are both for the chlorination of meta-cresol. All four catalysts show improvements over the use of diphenyl sulphide as a catalyst. Table E below, which illustrates reactions in which no AlCl_3 is present, shows that reducing the temperature of the reaction to 13°C increases the para:ortho ratio and the yield of para-mono-chlorinated product. This reaction temperature is possible as meta-cresol has a melting point of 8 - 10°C.

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Table C

| catalyst | mol% ortho-chloro meta-cresol | mol % meta-cresol | mol % para-chloro meta-cresol | p/o ratio | mass balance % |
|---------------------------|----------------------------------|----------------------|----------------------------------|--------------|-------------------|
| no catalyst | 10.4 | 10.3 | 79.3 | 7.7 | 95.4 |
| diphenyl sulfide | 14.8 | 15.8 | 69.4 | 4.7 | 86.4 |
| di-iso-propyl sulfide | 8.0 | 14.3 | 77.7 | 9.7 | 91.8 |
| di-n-butyl sulfide | 9.6 | 9.1 | 81.3 | 8.4 | 94.0 |
| ethyl phenyl sulfide | 12.3 | 25.1 | 62.6 | 5.1 | 79.0 |
| iso-propyl phenyl sulfide | 12.3 | 25.2 | 62.5 | 5.1 | 82.5 |

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Table D

| catalyst | mol% ortho-chloro meta-cresol | mol % meta-cresol | mol % para-chloro meta-cresol | p/o ratio | mass balance % |
|---------------------------|----------------------------------|----------------------|----------------------------------|--------------|-------------------|
| diphenyl sulfide | 11.3 | 15.3 | 73.4 | 6.5 | 82.6 |
| di-iso-propyl sulfide | 5.5 | 5.4 | 89.1 | 16.1 | 93.2 |
| di-n-butyl sulfide | 5.2 | 12.1 | 82.7 | 15.9 | 88.6 |
| ethyl phenyl sulfide | 8.6 | 16.8 | 74.6 | 8.7 | 85.3 |
| iso-propyl phenyl sulfide | 8.6 | 17.6 | 73.8 | 8.5 | 86.0 |

Table E

| catalyst | mol% ortho-chloro meta-cresol | mol % meta-cresol | mol % para-chloro meta-cresol | p/o ratio | mass balance % |
|--------------------|----------------------------------|----------------------|----------------------------------|--------------|-------------------|
| diphenyl sulfide | 11.2 | 11.4 | 77.4 | 7.0 | 87.0 |
| di-n-butyl sulfide | 6.2 | 7.2 | 86.6 | 13.8 | 91.4 |

Comparative Example 3

5 Tables F and G below illustrate the use of the same four sulphur-containing catalysts as in Comparative Example 2 above, respectively with (Table F) and without (Table G) the presence of AlCl_3 , in comparison with no catalyst and diphenyl sulphide for the chlorination of meta-xylenol. Again, all four catalysts show improvements over the use of diphenyl sulphide as a catalyst. This reaction has to be carried out at 80°C , as meta-xylenol has a high melting point of 66°C .

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Table E

| catalyst | mol% meta-xylene | mol % ortho-chloro meta-xylene | mol % para-chloro meta-xylene | mol% di-chloro meta-xylene | mol% tri-chloro meta-xylene | p/o ratio | mass balance % |
|-----------------------|---------------------|-----------------------------------|----------------------------------|-------------------------------|--------------------------------|--------------|-------------------|
| no catalyst | 19.0 | 8.7 | 68.9 | 3.4 | - | 7.9 | 98.7 |
| diphenyl sulfide | 20.6 | 21.5 | 49.0 | 8.9 | - | 2.3 | 100.0 |
| di-n-butyl sulfide | 25.3 | 13.0 | 48.6 | 13.1 | - | 3.7 | 95.6 |
| di-iso-propyl sulfide | 24.4 | 12.0 | 55.3 | 8.3 | - | 4.6 | 93.8 |
| ethyl phenyl sulfide | 40.9 | 12.1 | 25.9 | 19.7 | 1.4 | 2.5 | 98.0 |

Table G

| catalyst | mol% meta-xylene | mol % ortho-chloro meta-xylene | mol % para-chloro meta-xylene | mol% di-chloro meta-xylene | mol% tri-chloro meta-xylene | p/o ratio | mass balance % |
|-----------------------|---------------------|-----------------------------------|----------------------------------|-------------------------------|--------------------------------|--------------|-------------------|
| diphenyl sulfide | 15.6 | 15.9 | 58.3 | 10.2 | - | 3.7 | 100.0 |
| di-n-butyl sulfide | 36.0 | 8.0 | 40.1 | 14.2 | 1.7 | 5.1 | 94.1 |
| di-iso-propyl sulfide | 32.0 | 8.4 | 51.6 | 7.2 | 0.8 | 6.1 | 92.7 |
| ethyl phenyl sulfide | 47.0 | 5.9 | 26.7 | 16.3 | 4.1 | 4.6 | 98.5 |

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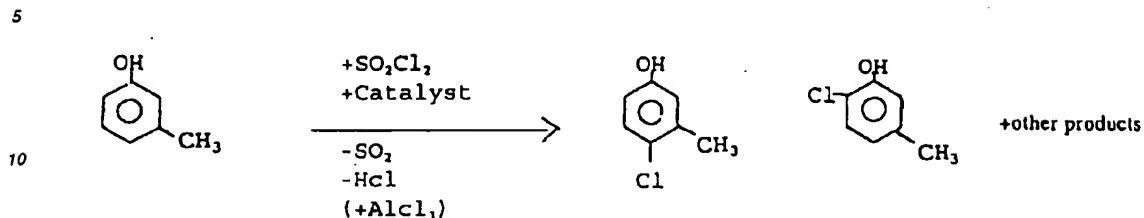
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Comparative Example 4 and Examples 10 to 22

In the following Comparative Example 4 and Examples 10 to 22 the following reaction:

Comparative Example 4

20 The results in Table H below illustrate the effects of slightly varying the reaction temperature in the absence of any catalyst. They provide a baseline against which to compare the results of the following example. There is no significant difference in the effectiveness of the catalyst over the small range of temperatures shown.

Table H

| temp. °C | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance |
|----------|-----------|---------|-----------|-----------|--------------|
| 18 | 9.3 | 4.5 | 86.2 | 9.3 | 97.7 |
| 18 | 9.4 | 6.9 | 83.7 | 8.9 | 100.0 |
| 19 | 9.2 | 8.7 | 82.1 | 8.9 | 98.0 |
| 23 | 9.8 | 9.6 | 80.8 | 8.3 | 97.2 |
| 25 | 9.4 | 10.2 | 80.4 | 8.5 | 99.8 |

Example 10

35 In this example (see Tables 10a and 10b below) the reaction is catalysed by a selection of symmetrical dialkyl sulphides, respectively in the absence (Table 10a) and presence (Table 10b) of AlCl_3 . As in Example 1 above, the para:ortho ratio of monochlorometa-cresol (CMC) peaks at an overall chain length of C_8 to C_{10} . The mol% of parachlorometa-cresol (PCMC) also follows a similar trend.

Table 10a

| alkyl chain | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance |
|-------------|-----------|---------|-----------|-----------|--------------|
| n-propyl | 8.2 | 5.7 | 86.1 | 10.5 | 97.8 |
| n-butyl | 6.4 | 5.8 | 87.8 | 13.7 | 90.0 |
| n-pentyl | 7.0 | 3.6 | 89.4 | 12.8 | 95.2 |
| n-hexyl | 7.9 | 5.4 | 86.7 | 11.0 | 95.7 |

Table 10b

| alkyl chain | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|-------------|-----------|---------|-----------|-----------|----------------|
| n-propyl | 6.3 | 5.9 | 87.8 | 14.0 | 95.2 |
| n-butyl | 5.4 | 1.1 | 93.5 | 17.3 | 99.7 |
| n-pentyl | 5.8 | 4.1 | 90.1 | 15.5 | 94.7 |

Table 10b (continued)

| alkyl chain | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|-------------|-----------|---------|-----------|-----------|----------------|
| n-hexyl | 5.6 | 4.5 | 89.9 | 16.1 | 93.0 |

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Synthesis Example 1

Various unsymmetrical dialkyl sulphides are prepared according to the synthesis(es) described earlier.

The synthesis of Compound 1 (methyl nonyl sulphide) in more detail is as follows. Iodomethane (12.8g, 90mmol), sodium hydroxide (6g, 150mmol), water (100ml), benzene (80ml) and methyltrioctylammonium chloride (200mg) are mixed and the system degassed with N₂ (60 minutes). Nonanethiol (14.44g, 90mmol) is added and the reaction is stirred for 24 hours at room temperature. The two layers are then separated and washed with benzene (2 x 10ml). The organic phases are combined and dried over magnesium sulphate. The solid is filtered off and the filtrate concentrated under atmospheric pressure (80°C). The reaction gives compound 1 (11.41g crude reaction mixture). A Kugelrohr (bulb to bulb) distillation is carried out at 0.8mbar, with the fraction at 66°C being pure methyl nonyl sulphide, isolated in a yield of 43%. The other three syntheses follow the same method.

Table I below illustrates four of these syntheses, including the isolated yield of the desired product. These relatively poor yields are due to the lack of exclusion of oxygen from the reaction apparatus. Compound 4 can be synthesised under a nitrogen atmosphere to give an improved yield of 72%.

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Table I

| compound number | starting materials | product | isolated yield % |
|-----------------|--|----------------------------------|------------------|
| 1 | CH ₃ -I, C ₉ H ₁₉ -SH | C ₁ -S-C ₉ | 43 |
| 2 | C ₈ H ₁₇ -Cl, C ₂ H ₅ S-SH | C ₂ -S-C ₈ | 16 |
| 3 | C ₇ H ₁₅ -Cl, C ₃ H ₇ -SH | C ₃ -S-C ₇ | 27 |
| 4 | C ₄ H ₉ -Br, C ₆ H ₁₃ -SH | C ₄ -S-C ₆ | 72 |

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Example 11

Table 11 below presents the data obtained for the chlorination of meta-cresol utilising the compounds 1 to 4 (see Example 10) and di-n-pentyl sulphide as catalysts in the absence of AlCl₃. The results show that the position of the sulphur within the thia-alkane chain is not crucial. Most of the para:ortho product ratios are between 10 and 12, with the best result of 12.8 using di-n-pentyl sulphide.

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Table 11

| compound | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance |
|----------------------------------|-----------|---------|-----------|-----------|--------------|
| C ₁ -S-C ₉ | 7.6 | 14.5 | 77.9 | 10.3 | 100.0 |
| C ₂ -S-C ₈ | 7.0 | 8.0 | 85.0 | 11.4 | 100.0 |
| C ₃ -S-C ₇ | 6.9 | 8.9 | 84.2 | 12.2 | 86.8 |
| C ₄ -S-C ₅ | 8.5 | 10.0 | 81.5 | 9.6 | 85.7 |
| C ₅ -S-C ₅ | 7.0 | 3.6 | 89.4 | 12.8 | 95.2 |

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Example 12

All the catalysts used in this example were commercially available and are used without further purification. The catalysts are listed in Tables 12a and 12b below in order of increasing steric hindrance around the sulphur atom. The unbranched dialkyl sulphide is the compound with the least steric hindrance, closely followed by n-butyl iso-butyl sulphide. These are followed by the n-butyl sec-butyl sulphide and finally n-butyl tert-butyl sulphide, both having steric hindrance at the α -carbon. The results further reinforce the theory that the steric bulk of the substituent groups is the parameter which primarily controls the effectiveness of the catalyst.

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Table 12a

| compound | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|----------------------------|-----------|---------|-----------|-----------|----------------|
| di-n-butyl sulfide | 7.1 | 7.1 | 85.8 | 12.1 | 96.6 |
| n-butyl iso-butyl sulfide | 8.3 | 6.2 | 85.5 | 10.3 | 96.1 |
| n-butyl sec-butyl sulfide | 7.6 | 8.3 | 84.1 | 11.1 | 95.6 |
| n-butyl tert-butyl sulfide | 13.5 | 9.4 | 77.1 | 5.7 | 88.7 |

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Table 12b

| compound | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|----------------------------|-----------|---------|-----------|-----------|----------------|
| di-n-butyl sulfide | 5.4 | 1.1 | 93.5 | 17.3 | 99.7 |
| n-butyl iso-butyl sulfide | 5.3 | 3.8 | 90.9 | 17.2 | 96.0 |
| n-butyl sec-butyl sulfide | 5.1 | 7.8 | 87.1 | 17.1 | 96.4 |
| n-butyl tert-butyl sulfide | 9.7 | 6.3 | 84.0 | 8.7 | 90.6 |

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Example 13

Tables 13a and 13b below illustrate the use of three sulphur-containing catalysts with the sulphur atom in three different oxidation states, respectively in the absence (Table 13a) and presence (Table 13b) of AlCl_3 . The effectiveness of the catalyst decreases as the oxidation state of the sulphur atom increases.

Table 13a

| catalyst | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--------------------------|-----------|---------|-----------|-----------|----------------|
| Bu_2S | 7.1 | 7.1 | 85.8 | 12.1 | 96.6 |
| Bu_2SO | 9.3 | 5.0 | 85.7 | 9.2 | 79.4 |
| Bu_2SO_2 | 10.1 | 6.0 | 83.9 | 8.3 | 97.4 |

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Table 13b

| oxidation state | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--------------------------|-----------|---------|-----------|-----------|----------------|
| Bu_2S | 5.4 | 1.1 | 93.5 | 17.3 | 99.7 |
| Bu_2SO | 7.2 | 12.5 | 80.3 | 11.2 | 86.4 |
| Bu_2SO_2 | 10.0 | 2.5 | 87.5 | 8.7 | 95.6 |

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Example 14

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Tables 14a and 14b below illustrate the use of different amounts of di-n-butyl sulphide (between 0.2mmol and 10mmol), respectively in the absence and presence of AlCl_3 . The most effective amount is when there is about 2mol% of catalyst in relation to the amount of meta-cresol in the reaction mixture.

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Table 14a

| amount of catalyst mmol/100 mmol MC | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--|--------------|---------|--------------|--------------|-------------------|
| 0.2 | 11.8 | 8.4 | 79.8 | 6.8 | 90.5 |
| 0.4 | 9.9 | 4.6 | 85.5 | 8.7 | 95.3 |
| 0.5 | 9.5 | 5.0 | 85.5 | 9.0 | 95.2 |

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Table 14a (continued)

| amount of catalyst mmol/100 mmol MC | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--|--------------|---------|--------------|--------------|-------------------|
| 5 | 1.3 | 7.2 | 6.5 | 86.3 | 12.0 |
| | 2.7 | 7.1 | 7.1 | 85.8 | 12.1 |
| | 3.0 | 7.4 | 6.1 | 86.5 | 11.7 |
| | 5.4 | 7.3 | 7.7 | 85.0 | 11.6 |
| | 8.0 | 7.9 | 6.3 | 85.8 | 10.9 |
| | 10.0 | 9.3 | 8.2 | 82.5 | 8.9 |
| 10 | | | | | |
| 15 | | | | | |

Table 14b

| amount of catalyst mmol/100 mmol MC | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--|--------------|---------|--------------|--------------|-------------------|
| 20 | 0.2 | 6.8 | 11.1 | 82.1 | 12.1 |
| | 0.4 | 5.2 | 5.1 | 89.7 | 16.6 |
| | 0.5 | 5.2 | 5.3 | 89.5 | 17.2 |
| | 1.3 | 5.4 | 6.3 | 88.3 | 16.3 |
| | 2.7 | 4.8 | 10.2 | 85.0 | 17.7 |
| | 3.0 | 5.6 | 11.3 | 83.1 | 14.8 |
| | 5.4 | 7.2 | 6.5 | 86.3 | 12.0 |
| | 10.0 | 6.0 | 13.6 | 80.4 | 13.4 |
| 25 | | | | | |
| 30 | | | | | |

Examples 15 to 18

The following Examples 15 to 18 all use di-n-butyl sulphide as the sulphur-containing catalyst.

Example 15

Table 15 below shows the results of the use of three different Lewis acids as co-catalysts for the chlorination reaction. AlCl_3 performs best, but both FeCl_3 and ZnCl_2 can be used as co-catalysts and result in good paraselectivities.

Table 15

| Lewis acid | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|-----------------|-----------|---------|-----------|-----------|----------------|
| AlCl_3 | 4.4 | 16.2 | 79.4 | 18.3 | 98.6 |
| FeCl_3 | 5.2 | 10.0 | 84.8 | 16.3 | 93.0 |
| ZnCl_2 | 5.7 | 7.0 | 87.3 | 15.3 | 95.3 |

Example 16

55 In this example (see Table 16 below) the amount of AlCl_3 present in the reaction mixture is altered between 0.8mmol and 11.3mmol. The most effective amount is about 4mol% in relation to the amount of meta-cresol present in the reaction mixture.

Table 16

| amount AlCl_3 mmol /100 mmol MC | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--|-----------|---------|-----------|-----------|----------------|
| 0.8 | 6.9 | 2.8 | 90.3 | 13.1 | 92.6 |
| 1.5 | 7.3 | 2.1 | 90.6 | 12.4 | 90.6 |
| 2.3 | 7.3 | 2.6 | 90.1 | 12.4 | 93.5 |
| 3.0 | 7.0 | 9.1 | 83.9 | 12.0 | 93.3 |
| 3.8 | 4.4 | 16.2 | 79.4 | 18.0 | 98.6 |
| 4.5 | 5.5 | 7.7 | 86.8 | 15.8 | 84.9 |
| 5.3 | 6.9 | 13.1 | 80.0 | 11.7 | 88.6 |
| 11.3 | 10.4 | 7.9 | 81.7 | 7.9 | 74.3 |

Example 17

Table 17 below illustrates the effect of changing the amount of sulphuryl chloride added to the reaction mixture, in the absence of AlCl_3 . As with Example 5 above, the optimum amount of sulphuryl chloride is about 20mol% excess in relation to the amount of meta-cresol present; this is where the concentration of parachlorometa-cresol peaks.

Table 17

| amount of SO_2Cl_2 mmol /100 mmol MC | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|--|------------------|------------------|-------------------|-----------|----------------|
| 80 | 5.9 | 33.5 | 60.6 | 10.3 | 97.1 |
| 90 | 6.3 | 22.7 | 71.0 | 11.3 | 95.5 |
| 100 | 7.3 | 12.9 | 79.8 | 10.9 | 92.2 |
| 110 | 7.1 | 7.1 | 85.8 | 12.1 | 96.6 |
| 120 | 7.1 | 6.2 | 86.7 | 12.2 | 100.0 |
| 150 | 3.4 ^a | 0.2 ^a | 68 ^a | 20.0 | 71.6 |
| 200 | 0.9 ^a | - | 33.2 ^a | 36.9 | 34.1 |

^aAbsolute yields quoted rather than normalised proportions.

Example 18

Tables 18a and 18b below show the effect of varying the temperature of the reaction between 19°C and 80°C, respectively in the absence (Table 18a) and presence (Table 18b) of AlCl_3 . As in Example 4 above, a lower temperature is preferred.

Table 18a

| temperature °C | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|----------------|-----------|---------|-----------|-----------|----------------|
| 19 | 7.1 | 7.1 | 85.7 | 12.1 | 96.6 |
| 30 | 8.9 | 9.1 | 82.0 | 9.2 | 96.4 |
| 40 | 10.7 | 9.1 | 80.2 | 7.5 | 93.8 |
| 50 | 12.3 | 14.1 | 73.6 | 6.0 | 87.5 |
| 60 | 14.4 | 15.3 | 70.3 | 4.9 | 86.2 |
| 70 | 16.5 | 16.7 | 66.8 | 4.0 | 88.4 |
| 80 | 17.8 | 20.9 | 61.3 | 3.4 | 87.0 |

Table 18b

| temperature °C | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|----------------|-----------|---------|-----------|-----------|----------------|
| 18 | 5.4 | 1.1 | 93.5 | 17.3 | 99.7 |
| 30 | 5.7 | 6.7 | 87.6 | 15.4 | 95.1 |
| 40 | 7.1 | 6.7 | 86.2 | 12.1 | 93.0 |
| 50 | 7.9 | 13.8 | 78.3 | 9.9 | 91.1 |
| 60 | 10.1 | 13.4 | 76.5 | 7.6 | 91.8 |
| 70 | 12.8 | 16.4 | 70.8 | 5.5 | 90.9 |
| 80 | 11.4 | 28.0 | 60.6 | 5.3 | 81.5 |

15 Synthesis Example 2

The following are the detailed methods for synthesising the dithia-alkanes used in Examples 19 to 22 which follow further below.

20 Method A: The alkanedithiol (HS-R⁵-SH) is placed in a 100ml flame-dried round bottom flask which is then fitted with a septum and flushed with N₂. Dry THF (20ml) is added via a dry syringe and the mixture is cooled to -78°C (cardice/acetone). Butyllithium is added via a dry syringe over 20 minutes and the mixture is stirred at -78°C for another 20 minutes. The reaction is allowed to warm up to ambient temperature. The bromoalkane (Br-R³) is added via a syringe and the reaction is stirred overnight at room temperature. The reaction mixture is then concentrated under reduced pressure (from a water pump) at 60°C and the residue is dissolved in a water-diethyl ether mixture (10ml, 1:1). The layers are separated and the water layer is washed with diethyl ether (2 x 15ml). The organic layers are combined and dried over MgSO₄ overnight. The solution is filtered and concentrated under reduced pressure. The residue is purified using a Kugelrohr (bulb to bulb) distillation.

25 Method B: The alkanethiol (HS-R³) is placed in a 100ml dried round bottom flask which is then fitted with a septum and flushed with N₂. Dry THF (20ml) is added via a dry syringe and the mixture is cooled to -78°C (cardice/acetone). Butyllithium is added via a dry syringe over 20 minutes and the mixture is stirred at -78°C for another 20 minutes. The reaction is allowed to warm up to ambient temperature. The dibromoalkane (Br-R⁵-Br) is added via a syringe and the reaction is stirred overnight at room temperature. The reaction mixture is then concentrated under reduced pressure (from a water pump) at 60°C and the residue is dissolved in a water-diethyl ether mixture (10ml, 1:1). The layers are separated and the water layer is washed with diethyl ether (2 x 15ml). The organic layers are combined and dried over MgSO₄ overnight. The solution is filtered and concentrated under reduced pressure. The residue is purified using a Kugelrohr (bulb to bulb) distillation.

30 Method C: The cyclic disulphide



45 (see below) is placed in a 100ml dried round bottom flask which is then fitted with a septum and flushed with N₂. Dry THF (20ml) is added via a dry syringe and the mixture is cooled to -78°C (cardice/acetone). The organolithium reagent (R³-Li) is added via a dry syringe over 20 minutes and the mixture is stirred at -78°C for another 20 minutes. The reaction is allowed to warm up to ambient temperature. The electrophile (R⁴-L) is added via a syringe and the reaction is stirred overnight at room temperature. The reaction mixture is then concentrated under reduced pressure (from a water pump) at 60°C and the residue is dissolved in a water-diethyl ether mixture (10ml, 1:1). The layers are separated and the water layer is washed with diethyl ether (2 x 15ml). The organic layers are combined and dried over MgSO₄ overnight. The solution is filtered and concentrated under reduced pressure. The residue is purified using a Kugelrohr (bulb to bulb) distillation.

50 Two of the required cyclic disulphides, 1,2-dithiane and 1,2-dithiacyclooctane, for Method C above are synthesised as follows.

55 1,2-Dithiane (Compound 28): Triethylamine (42.5g, 400mmol) is dissolved in dichloromethane (400ml) and cooled to 0°C in an ice bath. 1,4-Butanedithiol (25g, 200mmol) and iodine (51.9g, 400mmol) are added simultaneously so that the solution turns slightly yellow and the reaction temperature is below 5°C. After the end of the addition the reaction mixture is washed with dilute sodium thiosulphate solution (10%, 50ml) and water (2 x 50ml). The organic layer is

separated and dried over magnesium sulphate overnight. The solid is filtered off and the solvent is evaporated (18mbar, 50°C). The reaction gives 1,2-dithiane (24.6g, 98% crude yield). The oil is dissolved in hexane (250ml) and recrystallised (at -78°C) as a yellow solid (15.40g, 63% isolated yield). The compound is unstable and is best stored in a brown jar in the dark and cold. Its characterising spectroscopic data are: δ_H 1.97 (4H, s, CH_2CH_2S), 2.85 (4H, s, CH_2S).

5 1,2-Dithiacyclooctane (Compound 29): Triethylamine (33.9g, 332mmol) is dissolved in dichloromethane (400ml) and cooled to 0°C in an ice bath. 1,6-Hexanedithiol (25g, 166mmol) and iodine (42g, 332mmol) are added simultaneously so that the solution turns slightly yellow and the reaction temperature is below 5°C. After the end of the addition the reaction mixture is washed with dilute sodium thiosulphate solution (10%, 50ml) and water (2 x 50ml). The organic layer is separated and dried over magnesium sulphate overnight. The solid is filtered off and the solvent is evaporated (18mbar, 50°C). The reaction gives 1,2-dithiacyclooctane (12.41g, 88% crude yield). The oil is purified by Kugelrohr distillation (at 0.1mbar). The fraction at 120°C is the pure compound, isolated in a yield of 68%. Its characterising spectroscopic data are δ_H 1.72 (4H, m, $SCH_2CH_2CH_2$), 1.93 (4H, m, SCH_2CH_2), 2.78 (4H, m, SCH_2); δ_c 24.52 ($SCH_2CH_2CH_2$), 25.52 (SCH_2CH_2), 37.97 (SCH_2); EI m/z (%), $M^+ = 148$ (50), $M^+ = 55$ (100), $M^+ = 41$ (75).

10 Below are detailed the syntheses of Compounds 5 to 27 and compounds 30 to 40.

15 2,7-Dithiaoctane (Compound 5): The reaction is carried out as described in Method C using 1,2-dithiane (3.00 g, 25 mmol), methyl lithium (18.0 ml, 25 mmol, 1.4 M) and iodomethane (3.55 g, 25 mmol) as reagents. The reaction gives 2,7-dithiaoctane (3.26 g, 85.9% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (2.980 g) with a boiling point of 45°C is pure 2,7-dithiaoctane, isolated in a yield of 79.5%. Its characterising spectroscopic data are δ_H 1.71 (4H, m, SCH_2), 2.11 (6H, s, SCH_3), 2.52 (4H, m, SCH_2CH_2); δ_c 15.46 (CH_3), 28.01 (SCH_2), 33.76 (SCH_2CH_2). Elemental analysis found: C, 48.16; H, 9.53. $C_6H_{14}S_2$ requires C, 47.95; H, 9.39%.

20 2,8-Dithianonane (Compound 6): The reaction is carried out as described in Method A using 1,5-pentanedithiol (2.04g, 15 mmol), n-butyllithium (12 ml, 30 mmol, 2.5 M) and iodomethane (4.26 g, 30 mmol) as reagents. The reaction gives 2,8-dithianonane (1.98 g, 79% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (1.923 g) with a boiling point of 75°C is 2,8-dithianonane, isolated in a yield of 78%. Its characterising spectroscopic data are: δ_H 1.52 (2H, m, $SCH_2CH_2CH_2$), 1.62 (4H, m, SCH_2CH_2), 2.10 (6H, s, CH_3), 2.50 (4H, m, SCH_2); δ_c 15.52 (CH_3), 27.90 ($SCH_2CH_2CH_2$), 28.74 (SCH_2CH_2), 34.08 (SCH_2). Elemental analysis found: C, 51.08, H, 9.87. $C_7H_{16}S_2$ requires C, 51.17; H, 9.81%.

25 2,9-Dithiadecane (Compound 7): The reaction is carried out as described in Method C using DTCO (2.96 g, 20 mmol), methyl lithium (14.3 ml, 20 mmol, 1.4 M, in diethyl ether) and iodomethane (2.84 g, 20 mmol) as reagents. The reaction gives 2,9-dithiadecane (2.37 g, 67% crude yield). The Kugelrohr distillation is carried out at 0.3mbar and the fraction (1.963 g) with a boiling point of 90°C is pure 2,9-dithiadecane, isolated in a yield of 55%. Its characterising spectroscopic data are: δ_H 1.41 (4H, m, $SCH_2CH_2CH_2$), 1.61 (4H, m, SCH_2CH_2), 2.09 (6H, s, CH_3), 2.49 (4H, t, J7.4, SCH_2); δ_c 15.51 (CH_3), 28.36 ($SCH_2CH_2CH_2CH_2$), 28.99 (SCH_2CH_2), 34.17 (SCH_2). Elemental analysis found: C, 53.82; H, 10.38. $C_8H_{18}S_2$ requires C, 53.88; H, 10.17%.

30 2,9-Dithiaundecane (Compound 8): The reaction is carried out as described in Method B using methanethiol (2.00g, 40 mmol), n-butyllithium (16.7 ml, 42 mmol, 2.5 M) and 1,7-dibromoheptane (4.53 g, 17.6 mmol) as reagents. The reaction gives 2,9-dithiaundecane (3.33 g, 97% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (3.117 g) with a boiling point of 60°C is pure 2,9-dithiaundecane, isolated in a yield of 93%. Its characterising spectroscopic data are: δ_H 1.36 (6H, m, CH_2), 1.62 (4H, m, SCH_2CH_2), 2.10 (6H, s, CH_3), 2.49 (4H, t J7.4, SCH_2); δ_c 15.53 (CH_3), 28.65, 28.83 (1/2), 29.06, 34.21 (CH_2). Elemental analysis found: C, 56.18; H, 10.23. $C_9H_{20}S_2$ requires C, 56.19; H, 10.48%.

35 2,11-Dithiadodecane (Compound 9): The reaction is carried out as described in Method A using 1,8-octanedithiol (2.0 g, 11.2 mmol), n-butyllithium (9.0 ml, 22.4 mmol, 2.5 M) and iodomethane (3.20g, 22.4 mmol) as reagents. The reaction gives 2,11-dithiadodecane (1.44 g, 55% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (1.176 g) with a boiling point of 100°C is pure 2,11-dithiadodecane, isolated in a yield of 45%. Its characterising spectroscopic data are: δ_H 1.34 (8H, m, $SCH_2CH_2CH_2$), 1.60 (4H, m, SCH_2CH_2), 2.10 (6H, s, CH_3), 2.49 (4H, t, J7.4, SCH_2); δ_c 15.53 (CH_3), 28.72, 29.11 (CH_2), 34.26 (SCH_2).

40 2,13-Dithiatetradecane (Compound 10): The reaction is carried out as described in Method B using methanethiol (2.00 g, 40 mmol), n-butyllithium (16.7 ml, 20 mmol, 2.4 M) and 1,10-dibromodecane (6.00 g, 20 mmol) as reagents. The reaction gives 2,13-dithiatetradecane (4.69 g, 98% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (4.557 g) with a boiling point of 120°C is pure 2,13-dithiatetradecane, isolated in a yield of 97%. Its characterising spectroscopic data are: δ_H 1.34 (12H, m, CH_2), 1.60 (4H, m, SCH_2CH_2), 2.10 (6H, s, CH_3), 2.49 (4H, t J7.4, SCH_2); δ_c 15.53 (CH_3), 28.79, 29.15, 29.21, 29.44 (CH_2), 34.72 (SCH_2). Elemental analysis found: C, 61.39; H, 11.12. $C_{12}H_{26}S_2$ requires C, 61.47; H, 11.18%.

45 2,15-Dithiahexadecane (Compound 11): The reaction is carried out as described in Method B using methanethiol (2.00 g, 40 mmol), n-butyllithium (16.7 ml, 40 mmol, 2.4 M) and 1,12-dibromododecane (6.56 g, 20 mmol) as reagents. The reaction gives 2,15-dithiahexadecane as a pure white solid (4.784 g, 91% isolated yield). Its characterising spectroscopic data are: δ_H 1.33 (16H, m, CH_2), 1.60 (4H, m, SCH_2CH_2), 2.10 (6H, s, CH_3), 2.49 (4H, t J7.42, SCH_2); δ_c

15.53 (CH₃), 28.81, 29.16, 29.24, 29.50, 29.55 (CH₂), 34.28 (SCH₂). Elemental analysis found: C, 63.77; H, 12.15. C₁₄H₃₀S₂ requires C, 64.08; H, 11.53%.

5.10-Dithiatetradecane (Compound 12): The reaction is carried out as described in Method C using 1,2-dithiane (1 g; 8.4 mmol), butyllithium (3.2 ml, 8.6 mmol, 2.7 M) and 1-bromobutane (1.6 g, 8.4 mmol) as reagents. The reaction gives 5,10-dithiatetradecane (1.70 g, 87% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (1.620 g) with a boiling point of 235°C is pure 5,10-dithiatetradecane title compound, isolated in a yield of 83%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃CH₂), 1.41 (4H, m CH₃CH₂CH₂), 1.56 (4H, m, C₂H₅CH₂CH₂), 1.69 (4H, m, SCH₂CH₂), 2.52 (8H, m, SCH₂); δ_C 13.65 (CH₃CH₂), 21.98 (CH₃CH₂), 28.70 (C₂H₅CH₂), 31.64 (SCH₂CH₂), 31.64 (SCH₂CH₂), 31.74 (SCH₂), 31.76 (SCH₂); EI m/z (%) 234 (M⁺, 15), 177 (100), 145 (42), 121 (50); Cl m/z (%) 235 ([M⁺ + 1], 52), 177 (20), 145 (100).

5.11-Dithiapentadecane (Compound 13): The reaction is carried out as described in Method A using 1,5-pentanedithiol (2.73 g, 20 mmol), n-butyllithium (16.0 ml, 40 mmol, 2.5 M) and 1-bromobutane (5.50 g, 40 mmol) as reagents. The reaction gives 5,11-dithiapentadecane (4.02 g, 76% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (3.607 g) with a boiling point of 120°C is pure 5,11-dithiapentadecane, isolated in a yield of 73%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃), 1.51 (14H, m, CH₂), 2.51 (8H, m, SCH₂); δ_C 13.70 (CH₃), 22.02, 28.18 (1/2), 29.30, 31.77 (CH₂), 31.82, 31.95 (SCH₂). Elemental analysis found: C, 62.54; H, 11.68. C₁₃H₂₈S₂ requires C, 62.84; H, 11.36%.

5.13-Dithiaheptadecane (Compound 15): The reaction is carried out as described in Method B using 1-butanelithiol (3.61 g, 40 mmol), n-butyllithium (16 ml, 40 mmol, 2.5 M) and 1,7-dibromoheptane (5.16 g, 20 mmol) as reagents. The reaction gives 5,13-dithiaheptadecane (5.08 g, 90% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (4.850 g) with a boiling point of 120°C is pure 5,13-dithiaheptadecane, isolated in a yield of 88%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃), 1.38 (10H, m, SCH₂CH₂CH₂ and SCH₂CH₂CH₂CH₂), 1.58 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_C 13.73 (CH₃), 28.81, 28.88, 29.63 (CH₂), 31.82, 31.85, 32.12 (SCH₂). Elemental analysis found: C, 65.25; H, 11.82. C₁₅H₃₂S₂ requires C, 65.15; H, 11.66%.

5.14-Dithiaoctadecane (Compound 16): The reaction is carried out as described in Method A using 1,8-octanedithiol (2.0 g, 11.2 mmol), n-butyllithium (9 ml, 22 mmol, 2.5M) and 1-bromobutane (3.07 g, 22.4 mmol) as reagents. The reaction gives 5,14-dithiaoctadecane (2.91 g, 86% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (2.523 g) with a boiling point of 140°C is pure 5,14-dithiaoctadecane, isolated in a yield of 78%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃), 1.37 (12H, m, CH₂), 1.58 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂), δ_C 13.71 (CH₃), 22.04, 28.86, 29.12, 29.66 (CH₂), 31.81 (SCH₂CH₂), 32.12 (SCH₂).

5.16-Dithiaeicosane (Compound 17): The reaction is carried out as described in Method B using 1-butanelithiol (3.61 g, 40 mmol), n-butyllithium (16.0 ml, 40 mmol, 2.5 M) and 1,10-dibromodecane (6.00 g, 20 mmol) as reagents. The reaction gives 5,16-dithiaeicosane (6.11 g, 95% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (5.894 g) with a boiling point of 150°C is pure 5,16-dithiaeicosane, isolated in a yield of 93%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃), 1.28 (8H, m, CH₂), 1.39 (8H, m, SCH₂CH₂CH₂), 1.57 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_C 13.74, 22.07 (CH₂), 28.95-29.72 (CH₂), 31.84 (SCH₂), 32.17 (SCH₂). Elemental analysis found: C, 67.61; H, 12.07. C₁₈H₃₈S₂ requires C, 67.85; H, 12.02%.

5.18-Dithiadocosane (Compound 18): The reaction is carried out as described in Method B using 1-butanelithiol (3.61 g, 40 mmol), n-butyllithium (16 ml, 40 mmol, 2.5 M) and 1,12-dibromododecane (6.56 g, 20 mmol) as reagents. The reaction gives 5,18-dithiadocosane as a pure white solid (6.70 g), isolated in a yield of 97%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.33, CH₃), 1.26 (12H, m, SCH₂CH₂CH₂CH₂), 1.39 (8H, m, SCH₂CH₂CH₂), 1.58 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_C 13.71 (CH₃), 22.04 (SCH₂CH₂CH₂CH₃), 28.94, 29.24, 29.41, 29.51, 29.55, 29.71 (CH₂), 31.81 (SCH₂). Elemental analysis found: C, 69.15; H, 12.01. C₂₀H₄₂S₂ requires C, 69.29; H, 12.21%.

4.11-Dithiatetradecane (Compound 19): The reaction is carried out as described in Method A using 1,6-hexanedithiol (3.00 g, 20 mmol), n-butyllithium (16.0 ml, 40 mmol, 2.5 M) and 1-bromopropane (4.38 g, 29 mmol) as reagents. The reaction gives 4,11-dithiatetradecane (4.47 g, 93% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (4.322 g) with a boiling point of 125°C is pure 4,11-dithiatetradecane, isolated in a yield of 92%. Its characterising spectroscopic data are: δ_H 0.99 (6H, t, J7.35, CH₃), 1.40 (4H, m, CH₂), 1.61 (8H, m, SCH₂CH₂), 2.49 (8H, m, SCH₂); δ_C 13.55 (CH₃), 23.01 (CH₂CH₃), 28.54, 29.59 (CH₂), 32.02 (SCH₂), 34.21 (SCH₂). Elemental analysis found: C, 61.22; H, 11.22. C₁₂H₂₆S₂ requires C, 61.47; H, 11.18%.

5,12-Dithiahexamadecane (Compound 20): The reaction is carried out as described in Method C using DTCO (2.09 g, 14.1 mmol), n-butyllithium (1.5 ml, 14.1 mmol, 9.6 M) and 1-bromobutane (1.9 g, 14.1 mmol) as reagents. The reaction gives 5,12-dithiahexamadecane (2.98 g, 80% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (2.571 g) with a boiling point of 120°C is pure 5,12-dithiahexamadecane, isolated in a yield of 70%. Its characterising spectroscopic data are: δ_H 0.94 (6H, t, J7.3, CH₃), 1.41 (8H, m, SCH₂CH₂CH₂), 1.59 (8H, m, SCH₂CH₂), 2.50 (8H, t, J7.4, SCH₂); δ_C 13.69 (CH₃), 22.02 (CH₃CH₂), 28.51 (SCH₂CH₂CH₂), 29.54 (SCH₂CH₂), 31.79 (CH₃CH₂CH₂), 31.82 (SCH₂), 32.05 (CH₃CH₂CH₂CH₂S); EI m/z (%) 262 (M⁺, 10), 173 (35), 115 (50), 82 (45), 61

(100), 55 (65), 41 (50); Cl m/z (%), 263 ([M⁺ 1], 100), 173 (15).

6,13-Dithiaoctadecane (Compound 21): The reaction is carried out as described in Method A using 1,6-hexanedithiol (3.00 g, 20 mmol), n-butyllithium (16.0 ml, 40 mmol, 2.5 M) and 1-bromopentane (6.04 g, 20 mmol) as reagents. The reaction gives 6, 13-dithiaoctadecane (5.55 g, 92% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (5.230 g) with a boiling point of 150°C is pure 6,13-dithiaoctadecane, isolated in a yield of 90%. The characterising spectroscopic data are: δ_H 0.90 (6H, t, m, CH₃), 1.36 (12H, m, CH₂), 1.58 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_c 13.40 (CH₃), 22.32, 28.53, 29.40, 29.56, 31.13 (CH₂), 32.06, 32.14 (SCH₂). Elemental analysis found: C, 66.43; H, 11.52. C₁₆H₃₄S₂ requires C, 66.14; H, 11.79%.

8,15-Dithiadocosane (Compound 22): The reaction is carried out as described in Method A using 1,6-hexanedithiol (1.05 g, 7 mmol), n-butyllithium (5.6 ml, 14 mmol, 2.5 M) and 1-iodoheptane (3.165 g, 14 mmol) as reagents. The reaction gives 8,15-dithiadocosane (2.37 g, 96% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (2.129 g) with a boiling point of 175°C is pure 8,15-dithiadocosane title compound, isolated in a yield of 88%. Its characterising spectroscopic data are: δ_H 0.88 (6H, t J6.9, CH₃), 1.33 (20H, m, CH₂), 1.57 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_c 14.07 (CH₃), 22.60, 28.52, 28.91, 29.56, 29.71, 31.74 (CH₂), 32.06, 32.17 (SCH₂). Elemental analysis found: C, 69.31; H, 12.21. C₂₀H₄₂S₂ requires C, 69.29; H, 12.21%.

3,16-Dithia-octadecane (Compound 23): The reaction is carried out as described in Method B using ethanethiol (1.24 g, 20 mmol), n-butyllithium (8.3 ml, 20 mmol, 2.4M) and 1,12-dibromododecane (3.28 g, 10 mmol) as reagents. The reaction gives 3,16-dithia-octadecane (2.92 g, 94% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (2.554 g) with a boiling point of 155°C is pure 3,16-dithia-octadecane, isolated in a yield of 88%. Its characterising spectroscopic data are: δ_H 1.30 (22H, m, CH₂ and CH₃), 1.59 (4H, m, SCH₂CH₂), 2.53 (8H, m, SCH₂); δ_c 14.80 (CH₃), 25.89, 28.94, 29.24, 29.50, 29.54, 29.63 (CH₂), 31.94 (SCH₂). Elemental analysis found: C, 66.68; H, 11.66. C₁₆H₃₄S₂ requires C, 66.14; H, 11.79%.

4,17-Dithia-eicosane (Compound 24): The reaction is carried out as described in Method B using 1-propanethiol (1.52 g, 20 mmol), n-butyllithium (8.3 ml, 20 mmol, 2.4 M) and 1,12-dibromododecane (3.28 g, 10 mmol) as reagents. The reaction gives 4,17-dithia-eicosane (3.20 g, 93% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (2.708 g) with a boiling point of 180°C is the pure title compound, isolated in a yield of 85%. Its characterising spectroscopic data are: δ_H 0.92 (6H, t, J7.3, CH₃), 1.32 (16H, m, CH₂), 1.58 (8H, m, SCH₂CH₂), 2.49 (8H, m, SCH₂); δ_c 13.57 (CH₃), 23.02, 28.98, 29.27, 29.54, 29.59, 29.76, 32.12 (CH₂), 34.23 (SCH₂). Elemental analysis found: C, 67.97; H, 11.93. C₁₈H₃₈S₂ requires C, 67.85; H, 12.02%.

6,19-Dithiatetracosane (Compound 25): The reaction is carried out as described in Method B using 1-pentanethiol (2.08 g, 20 mmol), n-butyllithium (8.0 ml, 20 mmol, 2.5 M) and 1,12-dibromododecane (3.28 g, 10 mmol) as reagents. The reaction gives 6,19-dithiatetracosane (3.75 g, 95% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (3.155 g) with a boiling point of 160°C is pure 6,19-dithiatetracosane, isolated in a yield of 84%. Its characterising spectroscopic data are: δ_H 0.90 (6H, t J7.1, CH₃), 1.30 (24H, m, CH₂), 1.58 (8H, m, SCH₂CH₂), 2.50 (8H, t J7.1, SCH₂); δ_c 13.98 (CH₃), 22.32, 28.94, 29.25, 29.40, 29.51, 29.56, 29.71, 31.12 (CH₂), 32.12, 32.15 (SCH₂). Elemental analysis found: C, 70.60; H, 13.42. C₂₂H₄₆S₂ requires C, 70.52; H, 12.37%.

7,20-Dithiahexacosane (Compound 26): The reaction is carried out as described in Method B using 1-hexanethiol (2.43 g, 20 mmol), n-butyllithium (8.0 ml, 20 mmol, 2.5 M) and 1,12-dibromododecane (3.28 g, 10 mmol) as reagents. The reaction gives 7,20-dithiahexacosane (3.944 g, 91% crude yield). The Kugelrohr distillation is carried out at 0.2 mbar and the fraction (3.298 g) with a boiling point of 235°C is pure 7,20-dithiahexacosane, isolated in a yield of 82%. Its characterising spectroscopic data are: δ_H 0.89 (6H, t, J6.9, CH₃), 1.33 (28H, m, CH₂), 1.57 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_c 14.06 (CH₃), 22.58, 28.66, 28.97, 29.27, 29.53, 29.70, 29.72, 31.48 (CH₂), 32.17 (SCH₂). Elemental analysis found: C, 71.44; H, 13.73. C₂₄H₅₀S₂ requires C, 71.57; H, 12.51%.

8,21-Dithiaoctacosane (Compound 27): The reaction is carried out as described in Method B using 1-heptanethiol (2.73 g, 20 mmol), n-butyllithium (8.0 ml, 20 mmol, 2.5 M) and 1,12-dibromododecane (3.28 g, 10 mmol) as reagents. The reaction gives 8,21-dithiaoctacosane (4.34 g, 99% crude yield). The Kugelrohr distillation is carried out at 0.15 mbar and the fraction (3.641 g) with a boiling point of 255°C is pure 8,21-dithiaoctacosane, isolated in a yield of 85%. Its characterising spectroscopic data are: δ_H 0.88 (6H, m, CH₃), 1.32 (32H, m, CH₂), 1.57 (8H, m, SCH₂CH₂), 2.50 (8H, m, SCH₂); δ_c 14.07 (CH₃), 22.61, 28.92, 28.94, 29.26, 29.36, 29.51, 29.57, 29.65, 29.72, 31.74, 32.16 (CH₂). Elemental analysis found: C, 72.57; H, 14.13. C₂₆H₅₄S₂ requires C, 72.48; H, 12.63%.

2,7-Dithiaundecane (Compound 30): The reaction is carried out as described in Method C using 1,2-dithiane (3.00 g, 25 mmol), methylolithium (18 ml, 25 mmol, 1.4 M, in diethyl ether) and 1-bromobutane (3.43 g, 25 mmol) as reagents. The reaction gives 2,7-dithiaundecane (4.61 g, 81% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (3.502 g) with a boiling point of 100°C is pure 2,7-dithiaundecane, isolated in a yield of 73%. Its characterising spectroscopic data are: δ_H 0.92 (3H, t, J7.3, CH₃CH₂), 1.41 (2H, m, CH₃CH₂CH₂), 1.57 (2H, m, C₂H₅CH₂), 1.70 (4H, m, SCH₂CH₂), 2.10 (3H, s, SCH₃), 2.52 (6H, m, SCH₂); δ_c 13.72 (CH₃CH₂), 15.48 (SCH₃), 22.03 (CH₃CH₂), 28.04 (SCH₂CH₂), 28.16 (SCH₂CH₂), 28.60 (SCH₂CH₂), 31.65 (SCH₂), 33.79 (CH₃SCH₂); El m/z (%), 192 (M⁺, 30), 135 (95), 103 (55), 87 (50), 61 (100); Cl m/z (%), 210 ([M⁺ + 1 + NH₃], 10), 193 ([M⁺ + 1], 100), 145 (50), 103

(100).

Elemental analysis found: C, 55.98; H, 11.49. $C_9H_{20}S_2$ requires C, 56.19; H, 10.48%.

3,8-Dithiadodecane (Compound 31): The reaction is carried out as described in Method C using 1,2-dithiane (1.00g, 8.4 mmol), n-butyllithium (3.2 ml, 8.4 mmol, 2.7 M) and bromoethane (0.92 g, 8.4 mmol) as reagents. The reaction gives 3,8-dithiadodecane (1.85 g, 97% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (1.320 g) with a boiling point of 100°C is pure 3,8-dithiadodecane, isolated in a yield of 77%. Its characterising spectroscopic data are: δ_H 0.92 (3H, t, J7.3, $C_2H_5CH_3$), 1.26 (3H, t, J7.4, CH_3CH_2), 1.41 (2H, m, CH_3CH_2), 1.56 (2H, m, $SCH_2CH_2C_2H_5$), 1.69 (4H, m, SCH_2CH_2), 2.53 (8H, m, SCH_2); δ_c 13.68 ($CH_3C_2H_5$), 14.76 (SCH_2CH_3), 21.99 (CH_3CH_2), 25.83 ($C_2H_5CH_2$), 28.69 ($SCH_2CH_2CH_2$), 28.90 ($SCH_2CH_2CH_2$), 31.13 (SCH_2CH_2), 31.62 (SCH_2CH_2), 31.73 (SCH_2CH_2); EI m/z (%), 206 (M^+ , 20), 177 (85), 149 (85), 121 (100), 87 (85); Cl m/z (%), 207 ($[M^+ + 1]$, 100), 145 (80), 117 (100).

2,2-Dimethyl-3,8-dithiadodecane (Compound 32): The reaction is carried out as described in Method C using 1,2-dithiane (1.00 g, 8.4 mmol), tert-butyllithium (1.5 ml, 8.4 mmol, 5.6 M, in pentane) and 1-bromobutane (1.2 g, 8.4 mmol) as reagents. The reaction gives 2,2-dimethyl-3,8-dithiadodecane (1.93 g, 98% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (1.430 g) with a boiling point of 100°C is pure 2,2-dimethyl-3,8-dithiadodecane, isolated in a yield of 75%. Its characterising spectroscopic data are: δ_H 0.92 (3H, t, J7.3, CH_2CH_3), 1.32 (9H, s, $C(CH_3)_3$), 1.42 (2H, m, CH_3CH_2), 1.56 (2H, m, $C_2H_5CH_2$), 1.69 (4H, m, SCH_2CH_2), 2.53 (6H, m, SCH_2); δ_c 13.69 (CH_3CH_2), 21.99 (CH_3CH_2), 27.82 ($C_2H_5CH_2$), 28.95 ($SCH_2CH_2CH_2$), 29.07 ($SCH_2CH_2CH_2$), 30.95 ($C(CH_3)_3$), 31.62 (CH_2SCH_2), 31.74 (SCH_2), 41.83 ($C(CH_3)_3$); EI m/z (%), 234 (M^+ , 51), 177 (100), 121 (85), 87 (50), 57 (55), 41 (35); Cl m/z (%), 235 ($[M^+ + 1]$, 95), 177 (30), 145 (100).

1-Phenyl-2,7-dithiaundecane (Compound 33): The reaction is carried out as described in Method C using 1,2-dithiane (1.00 g, 8.4 mmol), n-butyllithium (3.2 ml, 8.4 mmol, 2.7 M) and benzyl bromide (1.44g, 8.4 mmol) as reagents. The reaction gives 1-phenyl-2,7-dithiaundecane (2.24 g, 79% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (1.475 g) with a boiling point of 235°C is pure 1-phenyl-2,7-dithiaundecane, isolated in a yield of 75%. Its characterising spectroscopic data are: δ_H 0.92 (3H, t, J7.3, CH_2CH_3), 1.32 (9H, s, $C(CH_3)_3$), 1.42 (2H, m, CH_3CH_2), 1.56 (2H, m, $C_2H_5CH_2$), 1.69 (4H, m, SCH_2CH_2), 2.53 (6H, m, SCH_2); δ_c 13.69 (CH_3CH_2), 21.99 (CH_3CH_2), 27.82 ($C_2H_5CH_2$), 28.95 ($SCH_2CH_2CH_2$), 29.07 ($SCH_2CH_2CH_2$), 30.95 ($C(CH_3)_3$), 31.62 (CH_2SCH_2), 31.74 (SCH_2), 41.83 ($C(CH_3)_3$); EI m/z (%), 234 (M^+ , 51), 177 (100), 121 (85), 87 (50), 57 (55), 41 (35); Cl m/z (%), 235 ($[M^+ + 1]$, 95), 177 (30), 145 (100).

1-Phenyl-1,6-dithiadecane (Compound 34): The reaction is carried out as described in Method C using 1,2-dithiane (1.00g, 8.4 mmol), phenyllithium (5.6 ml, 8.4 mmol, 1.5 M, in cyclohexane-diethyl ether 70/30) and 1-bromobutane (1.6g, 8.4 mmol) as reagents. The reaction gives 1-phenyl-1,6-dithiadecane (1.83 g, 77% crude yield). The Kugelrohr distillation is carried out at 0.4 mbar and the fraction (1.320 g) with a boiling point of 120-150°C is pure 1-phenyl-1,6-dithiadecane, isolated in a yield of 66.0%. Its characterising spectroscopic data are: δ_H 0.91 (3H, t, J7.3, CH_3CH_2), 1.41 (2H, m, CH_2CH_3), 1.59 (6H, m, SCH_2CH_2), 2.46 (6H, m, SCH_2), 3.69 (2H, s, $PhCH_2S$), 7.23 (1H, m, *p*-Ph), 7.30 (4H, m, Ph), δ_c 13.71 (CH_2CH_3), 22.02 (CH_2CH_3), 28.28 ($CH_2CH_2CH_3$), 28.64 (SCH_2CH_2), 30.83 ($SCH_2C_2H_5$), 31.66 (SCH_2), 31.78 (SCH_2), 36.20 (SCH_2Ph), 126.89 (*para*-Ph), 128.44 (*ortho*-Ph), 128.82 (*meta*-Ph), 138.52 (*ipso*-Ph); EI m/z (%), 214 (2), 177 (75), 121 (45), 91 (100); Cl m/z (%), 269 ($[M^+ + 1]$, 85), 179 (100), 145 (90).

1-Phenyl-8-methyl-1,6-dithianonane (Compound 35): The reaction is carried out as described in Method C using 1,2-dithiane (2.02 g, 15 mmol), phenyllithium (8.8ml, 16 mmol, 1.8 M, in cyclohexane-diethyl ether 70/30) and 1-bromo-2-methyl propane (2.06 g, 15 mmol) as reagents. The reaction gives 1-phenyl-8-methyl-1,6-dithianonane (3.35 g, 76% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (2.716 g) with a boiling point of 175°C is pure 1-phenyl-8-methyl-1,6-dithianonane, isolated in a yield of 71%. Its characterising spectroscopic data are: δ_H 0.97 (6H, d, J6.6, CH_3), 1.75 (5H, m, SCH_2CH_2 and CH), 2.38 (2H, d, J6.9, SCH_2CH ($CH_3)_2$), 2.50 (2H, t, J7.0, SCH_2CH_2), 2.93 (2H, t, J6.9, $PhSCH_2$), 7.16 (1H, m, *p*-Ph), 7.29 (4H, m, Ph); δ_c 22.05 (CH_3), 28.19 (SCH_2CH_2), 28.57 (SCH_2CH_2), 28.66 (CH), 32.17 (SCH_2), 33.18 (SCH_2), 44.42 ($PhSCH_2$), 125.79 (*para*-Ph), 128.83 (*Ph*), 129.03 (*Ph*), 136.58 (*ipso*-Ph). Elemental analysis found: C, 65.94; H, 8.70. $C_{14}H_{22}S_2$ requires C, 66.09; H, 8.71%.

1, 7-Diphenyl-1,6-dithiaheptane (Compound 36): The reaction is carried out as described in Method C using 1,2-dithiane (1.00 g, 8.4 mmol), phenyllithium (5.6 ml, 8.4 mmol, 1.5 M, in cyclohexane-diethyl ether 70/30) and benzyl bromide (1.4 g, 8.4 mmol) as reagents. The reaction gives 1,7-diphenyl-1,6-dithiaheptane (2.4 g, 99% crude yield). The Kugelrohr distillation is carried out at 0.05 mbar and the fraction (2.250 g) with a boiling point of 190-200°C is pure 1,7-diphenyl-1,6-dithiaheptane, isolated in a yield of 94%. Its characterising spectroscopic data are: δ_H 1.68 (4H, m, SCH_2CH_2), 2.39 (2H, m, CH_2SCH_2), 2.87 (2H, m, $PhSCH_2$), 3.67 (2H, s, SCH_2Ph), 7.16 (1H, m, *para*-PhS), 7.27 (9H, m, Ph); δ_c (1H / ^{13}C correlation spectra) 28.11 (SCH_2CH_2 , 2x), 30.70 (CH_2SCH_2); 30.77 ($PhSCH_2$), 33.15 ($PhCH_2S$), 125.86 (*para*-Ph), 126.94 (*para*-PhS), 128.50 - 129.21 (*Ph*), 136.60 (*ipso*-Ph), 138.46 (*ipso*-PhS); EI m/z (%), 211 (5), 197 ($[M^+ - CH_2Ph]$, 95), 91 (100); Cl m/z (%), 289 ($M^+ + 40$), 197 (35), 179 (100), 165 (85).

5,12-Dithianonadecane (Compound 37): The reaction is carried out as described in Method C using DTCO (1.24

g, 8.4 mmol), n-butyllithium (3.2 ml, 8.4 mmol), 2.7 M) and 1-iodoheptane (1.9 g, 8.4 mmol) as reagents. The reaction gives 5,12-dithianonadecane (2.261 g, 82% crude yield). The Kugelrohr distillation is carried out at 0.1 mbar and the fraction (1.557 g) with a boiling point of 170-180°C is pure 5,12-dithianonadecane, isolated in a yield of 61%. Its characterising spectroscopic data are: δ_H 0.90 (6H, m, CH_3), 1.30 (6H, m, $CH_3CH_2CH_2CH_2CH_2$), 1.41 (8H, m, $SCH_2CH_2CH_2$), 1.56 (8H, m, SCH_2CH_2), 2.50 (8H, m, SCH_2); δ_c ($^1H^{13}C$ correlation spectra) 13.71 (CH_3), 14.09 (CH_3), 22.05 ($SCH_2CH_2CH_2$), 22.62 (CH_3CH_2), 28.54 ($SCH_2CH_2CH_2$), 28.93 ($CH_3CH_2CH_2$ and $SCH_2CH_2CH_2$), 29.58 (SCH_2CH_2), 29.73 (SCH_2CH_2), 29.73 (SCH_2CH_2), 31.76 ($CH_3CH_2CH_2CH_2$), 31.82 (SCH_2CH_2), 31.85 (SCH_2), 32.08 (SCH_2); 32.20 (SCH_2); EI m/z (%) 346 (5, $C_7H_{15}S-C_6H_{12}S-C_7H_{15}$ as a minor impurity), 304 (M^+ , 15), 215 (65), 115 (100), 82 (70), 55 (95); CI m/z (%) 347 (see above 30), 305 ($[M^+ + H]$, 100), 263 (20).

1-Phenyl-2,9-dithiatridecane (Compound 38): The reaction is carried out as described in Method C using DTCO (1.24g, 8.4 mmol), n-butyllithium (3.2 ml, 8.4 mmol, 2.7 M) and benzyl bromide (1.4 g, 8.4 mmol) as reagents. The reaction gives 1-phenyl-2,9-dithiatridecane (2.19 g, 86% crude yield). The Kugelrohr distillation is carried out at 0.01 mbar and the fraction (1.117 g) with a boiling point of 175°C is pure 1-phenyl-2,9-dithiatridecane, isolated in a yield of 62%. Its characterising spectroscopic data are: δ_H 0.91 (3H, t, J 7.3, CH_3), 1.39 (6H, m, $SCH_2CH_2CH_2$), 1.56 (6H, m, SCH_2CH_2), 2.40 (2H, t, J 7.4, CH_2SCH_2Ph), 2.49 (4H, m, SCH_2), 3.69 (2H, s, SCH_2Ph), 7.24 (1H, m, p -Ph), 7.30 (4H, m, Ph); δ_c 13.73 (CH_3), 22.05 (CH_3CH_2), 28.45 ($SCH_2CH_2CH_2$), 28.48 ($SCH_2CH_2CH_2$), 28.48 ($SCH_2CH_2CH_2$), 29.06 ($CH_3CH_2CH_2CH_2S$), 30.21 (SCH_2CH_2), 31.27 (SCH_2CH_2), 31.82 (SCH_2), 31.85 (SCH_2), 32.05 (SCH_2), 36.29 (SCH_2Ph), 126.86 (*para*-Ph), 128.44 (*ortho*-Ph), 128.82 (*meta*-Ph), 138.62 (*ipso*-Ph). Elemental analysis found: C, 69.17; H, 10.04. $C_{26}H_{54}S_2$ requires C, 68.90; H, 9.50%.

Tables J, K and L below summarise the above syntheses.

Table J

| compound number | method ^a | product | isolated yield % |
|-----------------|---------------------|----------------------|------------------|
| 5 | C | $C_1-S-C_4-S-C_1$ | 80 |
| 6 | A | $C_1-S-C_5-S-C_1$ | 78 |
| 7 | C | $C_1-S-C_6-S-C_1$ | 55 |
| 8 | B | $C_1-S-C_7-S-C_1$ | 93 |
| 9 | A | $C_1-S-C_8-S-C_1$ | 45 |
| 10 | B | $C_1-S-C_{10}-S-C_1$ | 97 |
| 11 | B | $C_1-S-C_{12}-S-C_1$ | 91 |
| 12 | B/C | $C_4-S-C_4-S-C_4$ | 94/83 |
| 13 | B | $C_4-S-C_5-S-C_4$ | 73 |
| 14 | C | $C_4-S-C_6-S-C_4$ | 70 |
| 15 | B | $C_4-S-C_7-S-C_4$ | 88 |
| 16 | A | $C_4-S-C_8-S-C_4$ | 78 |
| 17 | B | $C_4-S-C_{10}-S-C_4$ | 93 |
| 18 | B | $C_4-S-C_{12}-S-C_4$ | 97 |

Table K

| compound number | method ^a | product | isolated yield % |
|-----------------|---------------------|----------------------|------------------|
| 19 | A | $C_3-S-C_6-S-C_3$ | 92 |
| 20 | C | $C_4-S-C_6-S-C_4$ | 70 |
| 21 | A | $C_5-S-C_6-S-C_5$ | 90 |
| 22 | A | $C_7-S-C_6-S-C_7$ | 88 |
| 23 | B | $C_2-S-C_{12}-S-C_2$ | 82 |
| 24 | B | $C_3-S-C_{12}-S-C_3$ | 85 |
| 25 | B | $C_5-S-C_{12}-S-C_5$ | 84 |
| 26 | B | $C_6-S-C_{12}-S-C_6$ | 82 |

Table K (continued)

| compound number | method ^a | product | isolated yield % |
|-----------------|---------------------|---|------------------|
| 27 | B | C ₇ S-C ₁₂ S-C ₇ | 85 |

5

Table L

| comp. number | RLi | disulfide | EX | product | crude yield % |
|--------------|-----|-----------------------|--------------|-----------------------------------|--|
| 10 | 5 | MeLi | 1,2-Dithiane | MeI | C ₁ -S-C ₄ -S-C ₁ |
| | 30 | MeLi | 1,2-Dithiane | BuBr | C ₁ -S-C ₄ -S-C ₄ |
| | 31 | BuLi | 1,2-Dithiane | EtBr | C ₄ -S-C ₄ -S-C ₂ |
| | 12 | BuLi | 1,2-Dithiane | BuBr | C ₄ -S-C ₄ -S-C ₄ |
| 15 | 32 | Bu ^{tert} Li | 1,2-Dithiane | BuBr | C ₄ ^{tert} -S-C ₄ -S-C ₄ |
| | 33 | Bu ⁿ Li | 1,2-Dithiane | PhCH ₂ Br | C ₄ -S-C ₄ -S-CH ₂ Ph |
| | 34 | PhLi | 1,2-Dithiane | BuBr | Ph-S-C ₄ -S-C ₄ |
| | 35 | PhLi | 1,2-Dithiane | Bu ^{iso} Br | Ph-S-C ₄ -S-C ₃ ^{iso} |
| 20 | 36 | PhLi | 1,2-Dithiane | PhCH ₂ Br | Ph-S-C ₄ -S-CH ₂ Ph |
| | 7 | MeLi | DTCO | MeI | C ₁ -S-C ₆ -S-C ₁ |
| | 20 | BuLi | DTCO | BuBr | C ₄ -S-C ₆ -S-C ₄ |
| | 37 | BuLi | DTCO | C ₇ H ₁₅ Br | C ₄ -S-C ₆ -S-C ₇ |
| 25 | 38 | BuLi | DTCO | PhCH ₂ Br | C ₄ -S-C ₆ -S-CH ₂ Ph |
| | | | | | 86 |

Examples 19 to 22

Example 19

Table 19 below illustrates the effectiveness of various catalysts of general formula (II), with both R³ and R⁴ being methyl groups, each R⁵ having a different chain length, in both the absence and presence of AlCl₃. The para:ortho ratios increase with the length of the R⁵ group, and the best results are achieved with C₁₀ to C₁₂.

Table 19

| Chlorination of <i>meta</i> -cresol in the presence of dithiaalkanes ^a | | | | | | |
|---|-------------------------------|---------|------------------------|------------------------|-----------|-----------------------------|
| catalyst | presence of AlCl ₃ | MC mol% | OCMC mol% ^b | PCMC mol% ^b | p/o ratio | mass balance % ^c |
| C ₁ -S-C ₄ -S-C ₁ | - | 6.2 | 15.2 | 70.6 | 4.6 | 92.0 |
| C ₁ -S-C ₄ -S-C ₁ | ✓ | 13.4 | 6.8 | 54.8 | 8.1 | 75.0 |
| C ₁ -S-C ₅ -S-C ₁ | - | 3.6 | 10.8 | 82.4 | 7.6 | 96.8 |
| | ✓ | 0.4 | 9.0 | 82.8 | 9.2 | 92.2 |
| C ₁ -S-C ₆ -S-C ₁ | - | 7.6 | 10.2 | 77.8 | 7.6 | 95.6 |
| | ✓ | 15.8 | 7.6 | 69.8 | 9.2 | 93.2 |
| C ₁ -S-C ₇ -S-C ₁ | - | 14.0 | 6.8 | 67.2 | 9.9 | 88.0 |
| | ✓ | 1.3 | 5.6 | 93.1 | 16.6 | 100.0 |
| C ₁ -S-C ₈ -S-C ₁ | - | 9.6 | 9.2 | 66.8 | 7.3 | 85.6 |
| | ✓ | 14.2 | 6.6 | 74.8 | 11.3 | 95.6 |

a) 100 mmol MC, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

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Table 19 (continued)

| Chlorination of <i>meta</i> -cresol in the presence of dithiaalkanes ^a | | | | | | |
|---|-------------------------------|---------|------------------------|------------------------|-----------|-----------------------------|
| catalyst | presence of AlCl ₃ | MC mol% | OCMC mol% ^b | PCMC mol% ^b | p/o ratio | mass balance % ^c |
| C ₁ -S-C ₁₀ -S-C ₁ | - | 5.0 | 7.8 | 82.9 | 10.6 | 95.7 |
| C ₁ -S-C ₁₀ -S-C ₁ | ✓ | - | 5.0 | 87.6 | 17.5 | 92.6 |
| C ₁ -S-C ₁₂ -S-C ₁ | - | 6.0 | 8.0 | 79.6 | 10.0 | 93.6 |
| C ₁ -S-C ₁₂ -S-C ₁ | ✓ | - | 5.2 | 84.8 | 16.3 | 90.0 |

a) 100 mmol MC, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

15 Example 20

20 Table 20 illustrates the effectiveness of various catalysts of general formula (II), with both R³ and R⁴ being n-butyl groups, each R⁵ having a different chain length, in both the absence and presence of AlCl₃. The para:ortho ratios generally increase with the length of the R⁵ group, and the best overall results (including a high yield of desired product) are achieved with C₁₀ to C₁₂.

Table 20

| Chlorination of <i>meta</i> -cresol in the presence of dithiaalkanes ^a | | | | | | |
|---|-------------------------------|---------|------------------------|------------------------|-----------|-----------------------------|
| catalyst | presence of AlCl ₃ | MC mol% | OCMC mol% ^b | PCMC mol% ^b | p/o ratio | mass balance % ^c |
| C ₄ -S-C ₄ -S-C ₄ | - | 11.8 | 14.2 | 67.3 | 4.7 | 93.3 |
| C ₄ -S-C ₄ -S-C ₄ | ✓ | 9.0 | 8.8 | 64.0 | 7.2 | 81.8 |
| C ₄ -S-C ₅ -S-C ₄ | - | 6.7 | 10.2 | 83.1 | 8.1 | 100.0 |
| C ₄ -S-C ₅ -S-C ₄ | ✓ | 0.6 | 6.5 | 86.8 | 13.4 | 93.9 |
| C ₄ -S-C ₆ -S-C ₄ | - | 5.4 | 9.6 | 77.6 | 8.1 | 92.6 |
| C ₄ -S-C ₆ -S-C ₄ | ✓ | 7.2 | 6.0 | 78.8 | 13.1 | 92.0 |
| C ₄ -S-C ₇ -S-C ₄ | - | 4.0 | 8.8 | 85.0 | 9.7 | 97.8 |
| C ₄ -S-C ₇ -S-C ₄ | ✓ | 10.6 | 3.2 | 72.4 | 22.7 | 86.2 |
| C ₄ -S-C ₈ -S-C ₄ | - | 9.6 | 6.8 | 76.8 | 11.3 | 93.2 |
| C ₄ -S-C ₈ -S-C ₄ | ✓ | 13.2 | 4.8 | 72.2 | 15.1 | 90.2 |
| C ₄ -S-C ₁₀ -S-C ₄ | - | 5.2 | 7.0 | 84.6 | 12.1 | 96.8 |
| C ₄ -S-C ₁₀ -S-C ₄ | ✓ | 1.8 | 4.8 | 92.8 | 19.3 | 99.4 |
| C ₄ -S-C ₁₂ -S-C ₄ | - | 3.5 | 6.9 | 89.6 | 13.0 | 100.0 |
| C ₄ -S-C ₁₂ -S-C ₄ | ✓ | - | 4.4 | 91.8 | 20.9 | 96.2 |

45 a) 100 mmol MC, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

Example 21

50 Table 21 below illustrates the effectiveness of various catalysts of general formula (II), with R⁵ being a straight chain C₁₂ group, R³ and R⁴ being a series of straight chain alkyl groups each with a different chain length, in both the absence and presence of AlCl₃. The best overall results are obtained using C₄-S-C₁₂-S-C₄ as the catalyst.

Table 21

| Chlorination of <i>meta</i> -cresol in the presence of dithiaalkanes ^a | | | | | | | |
|---|---|----------------------------------|---------|---------------------------|---------------------------|-----------|--------------------------------|
| | catalyst | presence of AlCl ₃ | MC mol% | OCMC mol% ^b | PCMC mol% ^b | p/o ratio | mass balance % ^c |
| 5 | C ₁ -S-C ₁₂ -S-C ₁ | - | 6.0 | 8.0 | 79.6 | 10.0 | 93.6 |
| | C ₁ -S-C ₁₂ -S-C ₁ | ✓ | - | 5.2 | 84.8 | 16.2 | 90.0 |
| 10 | C ₂ -S-C ₁₂ -S-C ₂ | - | 9.0 | 7.2 | 76.0 | 10.5 | 92.2 |
| | C ₂ -S-C ₁₂ -S-C ₂ | ✓ | 4.0 | 5.8 | 67.6 | 11.5 | 77.4 |
| 15 | C ₃ -S-C ₁₂ -S-C ₃ | - | 9.4 | 6.6 | 84.0 | 12.7 | 100.0 |
| | C ₃ -S-C ₁₂ -S-C ₃ | ✓ | 5.4 | 4.8 | 82.8 | 17.4 | 93.0 |
| 20 | C ₄ -S-C ₁₂ -S-C ₄ | - | 3.5 | 6.9 | 89.6 | 13.0 | 100.0 |
| | C ₄ -S-C ₁₂ -S-C ₄ | ✓ | - | 4.4 | 91.8 | 20.7 | 96.2 |
| 25 | C ₅ -S-C ₁₂ -S-C ₅ | - | 6.4 | 7.4 | 79.2 | 10.7 | 93.0 |
| | C ₅ -S-C ₁₂ -S-C ₅ | ✓ | 0.5 | 5.2 | 85.0 | 16.8 | 90.7 |
| 30 | C ₆ -S-C ₁₂ -S-C ₆ | - | 0.5 | 6.6 | 82.2 | 12.4 | 89.3 |
| | C ₆ -S-C ₁₂ -S-C ₆ | ✓ | 7.6 | 5.0 | 70.7 | 14.2 | 83.3 |
| 35 | C ₇ -S-C ₁₂ -S-C ₇ | - | 0.6 | 7.2 | 83.2 | 11.6 | 91.0 |
| | C ₇ -S-C ₁₂ -S-C ₇ | ✓ | 8.8 | 6.0 | 77.4 | 12.9 | 92.2 |

^a) 100 mmol MC, 110 mmol SO₂Cl₂, 4h, room temperature; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MC+OCMC+PCMC; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

Example 22

30 This example (see Table 22 below) illustrates the effect of changing the Lewis acid present in the reaction mixture, where the catalyst is C₄-S-C₁₂-S-C₄. As in Example 15 above, the most preferred co-catalyst is AlCl₃, though both FeCl₃ and ZnCl₂ perform well.

Table 22

| Lewis acid | OCMC mol% | MC mol% | PCMC mol% | p/o ratio | mass balance % |
|-----------------------|-----------|---------|-----------|-----------|----------------|
| AlCl ₃ | 4.6 | - | 95.4 | 20.7 | 96.2 |
| FeCl ₃ | 5.5 | 11.3 | 83.2 | 14.8 | 94.0 |
| ZnCl ₂ | 5.8 | 11.7 | 82.5 | 14.0 | 89.0 |
| 3 × ZnCl ₂ | 5.6 | 0.7 | 93.7 | 17.0 | 89.2 |

Scale-up Examples 1 and 2

45 In the following Scale-up Examples 1 and 2 the chlorination reaction of *meta*-cresol is scaled up seven-fold. The reaction is sampled continuously and a separation of the product mixture is attempted. The experiment is not quenched after 4 hours, but instead monitored for up to 25 hours.

Scale-up Example 1

50 In this example the catalyst used is di-*n*-butyl sulphide, and approximately 76g of *meta*-cresol is used. In order to simplify the reaction mixture, no AlCl₃ is added. The reaction is essentially finished after 4 hours and no further concentration changes take place after this time. The reaction mixture is separated by distillation under atmospheric pressure, using a 10cm Vigreux column. Separation of the di-*n*-butyl sulphide catalyst from the reaction mixture was not complete, because of the similar volatility of the catalyst and the products.

Scale-up Example 2

In this example the catalyst used is di-iso-propyl sulphide, which is more volatile than di-n-butyl sulphide. As in Scale-up Example 1, approximately 76g of meta-cresol is used, and the conditions used in that previous example apply (see Table M below for analysis of the fractions from the distillation). The higher volatility of the catalyst appears to improve its separation from the reaction mixture. All of the catalyst was recovered in Fraction 1, although it was not 100% pure.

Table M

| | boiling point °C | amount g | catalyst mol% | OCMC mol% | MC mol% | PCMC mol% |
|------------|------------------|----------|---------------|-----------|---------|-----------|
| Fraction 1 | 112-160 | 1.83 | 85.5 | 4.2 | 1.2 | 9.1 |
| Fraction 2 | 160-218 | 11.376 | traces | 30.9 | 19.9 | 49.2 |
| Fraction 3 | 218-235 | 15.292 | traces | 12.6 | 9.9 | 77.5 |
| Fraction 4 | 235-238 | 64.888 | - | 2.1 | 2.2 | 95.8 |

Example 23

This Example illustrates the use of various catalysts of general formula (I) in the chlorination of meta-xlenol, which is another phenol substrate within the scope of application of the invention. Results are given in Table 23 below, for both in the absence and presence of AlCl_3 and, for comparison, for the use of no catalyst at all.

Table 23

| Chlorination of <i>meta</i> -xlenol in the presence of dialkyl sulfides ^a | | | | | | | |
|--|-----------------------------|---------|------------------------|------------------------|------------------------|-----------|-----------------------------|
| catalyst | presence of AlCl_3 | MX mol% | OCMX mol% ^b | PCMX mol% ^b | DCMX mol% ^b | p/o ratio | mass balance % ^c |
| no catalyst | - | 18.8 | 8.6 | 68.0 | 3.4 | 7.9 | 98.8 |
| di-iso-propyl sulfide | - | 22.9 | 11.3 | 51.9 | 7.8 | 4.6 | 93.9 |
| di-iso-propyl sulfide | ✓ | 29.7 | 7.8 | 47.8 | 6.7 | 6.1 | 92.0 |
| di-n-butyl sulfide | - | 24.2 | 12.4 | 46.4 | 12.5 | 3.7 | 95.5 |
| di-n-butyl sulfide | ✓ | 33.9 | 7.5 | 37.9 | 13.4 | 5.1 | 92.7 |

a) 100 mmol MX, 110 mmol SO_2Cl_2 . 4h, 80°C; b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; c) sum of MX+OCMX+PCMX+DCMX; low mass balance indicates either physical loss of material or the production of other materials such as polychloro compounds.

Example 24

This Example illustrates the use of an exemplary catalyst of general formula II according to the invention, of the schematic formula $\text{C}_4\text{-S-C}_{12}\text{-S-C}_4$ (where the C_4 groups are n-butyl groups), in the chlorination of a variety of substrates within the scope of application of the invention. The results are given in Table 24 below.

Table 24

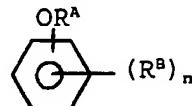
| Chlorination of various substrates using C ₄ -S-C ₁₂ -S-C ₄ as a catalyst in the presence of AlCl ₃ ^a | | | | | | | |
|--|------------|-------------------------------------|---|--|-----------|----------|--------------------------------|
| | substrate | starting mat. mol % ^b | ortho- chloro- comp. mol% ^b | para-chloro- comp. mol% ^b | p/o ratio | temp. °C | mass balance % ^c |
| 5 | phenol | 11.4 | 6.6 | 76.4 | 11.5 | 35 | 94.4 |
| 10 | anisole | 0.9 | 10.8 | 88.3 | 8.2 | 20 | 100 |
| 15 | m-xyleneol | 22.2 | 7.2 | 44.4 | 6.1 | 70 | 73.8 |

^a) 100 mmol substrate, 110 mmol SO₂Cl₂, 2.7 mmol C₄-S-C₁₂-S-C₄, 3.8 mmol AlCl₃, 4h, ^b) expressed as the absolute yield of the compounds listed, as determined by quantitative GC; ^c) sum of compounds listed; low mass balance indicates either physical loss of material or the production of other materials such as dichloro compounds.

Claims

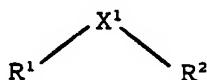
20 1. A process for the chlorination of an aromatic compound of the following formula (A):

(A)



25 wherein R^A is H or C₁ to C₁₂ alkyl, cycloalkyl, aryl, alkaryl, aralkyl or carboxyalkyl, the or each R^B independently is selected from H, C₁-C₄ alkyl (especially methyl), C₁-C₄ haloalkyl or polyhaloalkyl, e.g. C₁-C₄ perfluoroalkyl, C₁-C₄ alkoxy, C₅-C₁₂ aryl (e.g. phenyl), alkaryl or aralkyl, or halogen, n is an integer which is 0, 1 or 2, and the or each R^B, if present, may independently be attached at the ortho or the meta position, preferably at the meta-position, the said process comprising reacting the aromatic compound with a chlorinating agent in the presence of a sulphur-containing catalyst, optionally also in the presence of a Lewis acid co-catalyst of the formula MX_m, where: M is a metal or metalloid such as B, Al, Ga, In, Tl, Ge, Sn, Cd, Ni, Fe, Zn, Ti, Hg, La; X is an electronegative group such as F, Cl, Br, I, C₁-C₄ alkoxide, aryloxide e.g. phenoxide, carboxylate e.g. acetate, arene carboxylate e.g. benzoate, substituted carboxylate e.g. trifluoroacetate, C₁-C₄ alkanesulphonate, arenesulphonate or substituted sulphonate e.g. trifluoromethanesulphonate; and m is an integer which is preferably 1, 2, 3 or 4;

35 **characterised in that** the sulphur-containing catalyst is a compound according to the following formula (I) or formula (II):



(I)



(II)

40 in which: each of X¹, X², and X³ is independently selected from the group consisting of: S, SO, SO₂;

45 R¹ is selected from the group consisting of: optionally substituted straight or branched chain alkyl or alkanediyl having from 2 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;

5 R^2 is an optionally substituted straight or branched chain alkyl or alkanediyl group having from 1 to 20 carbon atoms;

10 R^3 and R^4 are each independently selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms, and optionally substituted aryl having from 5 to 20 carbon atoms;

15 R^5 is an optionally substituted straight or branched chain alkylene, arylene, alkarylene or arylalkylene group having from 1 to 20 carbon atoms;

20 wherein in the above definitions of R^1 , R^2 , R^3 , R^4 and R^5 the optional substituents may be independently selected from the following: halogen (e.g. F, Cl), hydroxy, amino, cyano, nitro, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl e.g. C_1 - C_4 perfluoroalkyl, C_1 - C_4 alkoxy, C_1 - C_4 alkoxy carbonyl.

25 2. A process according to claim 1, wherein the aromatic compound is phenol.

30 3. A process according to claim 1 or claim 2, wherein the chlorinating agent is sulphuryl chloride.

35 4. A process according to any one of claims 1 to 3, wherein the chlorination reaction is carried out in homogenous liquid phase, without the presence of added solvent.

40 5. A process according to any preceding claim, wherein the chlorination reaction is carried out at a temperature of below 35°C, preferably in the range from 15 to 30°C.

45 6. A sulphur-containing compound according to formula (I) or formula (II) as defined in claim 1, wherein X^1 , X^2 , X^3 , R^1 , R^2 , R^3 , R^4 and R^5 therein have the same meanings as in claim 1, for use as a catalyst in the chlorination of an aromatic compound according to formula (A) as defined in claim 1, wherein R^A , R^B and n therein have the same meanings as in claim 1, by a chlorinating agent.

50 7. A compound according to formula (I) as defined in claim 6, which is a symmetrical, unbranched dialkyl sulphide in which the alkyl groups R^1 and R^2 each independently contain from 2 to 16 carbon atoms, more preferably 4 or 5 carbon atoms each.

8. A compound according to formula (I) as defined in claim 6, which is a symmetrical, branched dialkyl sulphide in which the alkyl groups R^1 and R^2 each independently contain from 2 to 16 carbon atoms, more preferably 3 or 4 carbon atoms each.

9. A compound according to formula (I) as defined in claim 6, which is an unsymmetrical sulphide in which R^1 and R^2 are different, wherein one of R^1 and R^2 is *n*-butyl and the other of R^1 and R^2 contains from 2 to 4 carbon atoms.

10. A compound according to formula (I) as defined in claim 6, which is an unsymmetrical sulphide in which R^1 and R^2 are different, wherein one of R^1 and R^2 is phenyl and the other of R^1 and R^2 is an unbranched alkyl group having from 1 to 3 carbon atoms.

11. A compound according to formula (II) as defined in claim 6, wherein both of the groups X^2 and X^3 are S.

12. A compound according to formula (II) as defined in claim 6, wherein R^5 is an unbranched, unsubstituted alkane diyl group containing from 4 to 12 carbon atoms.

13. A compound according to formula (II) as defined in claim 6, wherein the groups R^3 and R^4 have the same carbon atom framework and both groups are unbranched and unsubstituted and independently contain from 1 to 7 carbon atoms.

14. A compound according to formula (II) as defined in claim 6, wherein the groups R^3 and R^4 have different carbon atom frameworks, R^3 being selected from the group consisting of: H, optionally substituted straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms and optionally substituted aryl having from 5 to 20 carbon atoms, and R^4 is different from R^3 and is selected from the group consisting of: optionally substituted

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straight or branched chain alkyl or alkanediyl having from 1 to 20 carbon atoms, optionally substituted straight or branched chain alkaryl or aralkyl having from 5 to 20 carbon atoms.

5 15. Use of a sulphur-containing compound according to any one of claims 6 to 14 as a catalyst in the chlorination of an aromatic compound of formula (A) as defined in claim 1 by a chlorinating agent.

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